rth Carolina Cancer Bulletin

s of North Carolina by the Division of Cancer Control of the North Carolina State Board with the Committee on Cancer Control of the North Carolina Medical Society and the of the American Cancer Society. Originally published by the Committee on Cancer of Society, with the financial aid of the Illinois Division of the American Cancer Society, ier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

NO. 1

NTRODUCTION

een written and published
tively little is of practical
ıary task confronting us
COGNITION of cancer.
nded to present *practical*
eryday practice. This first
ıst present statistical mat-
ıch statistics the seriousion, and the imperative
ɔn, can be demonstrated.
ırself—men busy with the
es—it is not striving for
ine medical writing.

bring you the **tools for**
:er which the sum of the
nembers makes available.
be presented must be di-
r with us in this—do not
ICER BULLETINS.
will bring you material
at you will wish to pre-
ind it profitable to turn

re punched for filing. A
ble for the asking.
h us in this fight against
t the most out of this
fellows in Illinois medi-
st card now, so that we
n which these bulletins

orrectly stated. No post-

.5 THE CANCER SITUATION TODAY?

et, none of the basic problems of cancer have
solved. Contributing factors are known, but
mechanism that changes "precancerous cells"
actual cancer, or activates the cancer poteninherent in each tissue, remains unknown.

Fortunately, this situation need not be of great concern to us for the present purpose. The approach here planned appears sound and practical, regardless of any theory or hypothesis on cancer. These are established facts:

(1) **Cancer is a curable disease,** provided it is recognized sufficiently early.

(2) There is still a wide gap between the number of cases that are **recognized in time and given early treatment,** and the considerably larger number that are properly diagnosed TOO LATE to be given effective treatment.

Here is the great opportunity of every general practitioner. It is he who sees the patient first.

If every patient above forty, who approaches the general practitioner, regardless of the complaint voiced, arouses the thought

WHEN THE PATIENT IS OVER FORTY
THINK OF CANCER FIRST

and is given the right examination, an infinitely larger number of cases will be recognized sufficiently early to cut cancer mortality considerably.

Such examinations and the proper history of the patient are not difficult. No greater skill is required than every medical man can muster. Many diagnostic means are at our disposal that are simple, not at all difficult. Their use is neither costly to the practitioner nor too time-consuming.

The real problem is that the signs and symptoms of early cancer are so few, and often so vague, that they will escape any except the most exacting investigation and the most thorough examination.

WHAT IS EARLY RECOGNITION?

After placing so much emphasis on the word "early," the demand for a definition is justified. Recognition is early when the cancer is discovered in a stage where it is eradicable – *completely* eradicable, to effect a cure, or *partially,* so that the patient's span of life may be lengthened materially.

There are, of course, some cancers which do not

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 1

BY WAY OF INTRODUCTION

A wealth of material has been written and published about cancer. Yet comparatively little is of practical applicability in the primary task confronting us today: the EARLIER RECOGNITION of cancer.

These bulletins are intended to present *practical* material, applicable in everyday practice. This first one, however, perforce must present statistical matter, since only through such statistics the seriousness of the cancer situation, and the imperative need for earlier recognition, can be demonstrated.

Written by men like yourself—men busy with the demands of their practices—it is not striving for beauty of language, for fine medical writing.

Rather, it endeavors to bring you the **tools for earlier recognition of cancer** which the sum of the experience of your fellow members makes available.

Part of the material to be presented must be didactic. We ask you to bear with us in this—do not skip any part of these CANCER BULLETINS.

Every succeeding issue will bring you material that you will treasure, that you will wish to preserve, to which you will find it profitable to turn time and again.

Hence, these bulletins are punched for filing. A three-ring binder is available for the asking.

If you are interested with us in this fight against cancer; if you wish to get the most out of this effort on the part of your fellows in Illinois medicine, **mail the enclosed post card now,** so that we can send you the binder in which these bulletins are to be kept.

Be sure your address is correctly stated. No postage is required.

WHAT IS THE CANCER SITUATION TODAY?

As yet, none of the basic problems of cancer have been solved. Contributing factors are known, but the mechanism that changes "precancerous cells" into actual cancer, or activates the cancer potential inherent in each tissue, remains unknown.

Fortunately, this situation need not be of great concern to us for the present purpose. The approach here planned appears sound and practical, regardless of any theory or hypothesis on cancer. These are established facts:

(1) **Cancer is a curable disease,** provided it is recognized sufficiently early.

(2) There is still a wide gap between the number of cases that are **recognized in time and given early treatment,** and the considerably larger number that are properly diagnosed TOO LATE to be given effective treatment.

Here is the great opportunity of every general practitioner. It is he who sees the patient first.

If every patient above forty, who approaches the general practitioner, regardless of the complaint voiced, arouses the thought

WHEN THE PATIENT IS OVER FORTY
THINK OF CANCER FIRST

and is given the right examination, an infinitely larger number of cases will be recognized sufficiently early to cut cancer mortality considerably.

Such examinations and the proper history of the patient are not difficult. No greater skill is required than every medical man can muster. Many diagnostic means are at our disposal that are simple, not at all difficult. Their use is neither costly to the practitioner nor too time-consuming.

The real problem is that the signs and symptoms of early cancer are so few, and often so vague, that they will escape any except the most exacting investigation and the most thorough examination.

WHAT IS EARLY RECOGNITION?

After placing so much emphasis on the word "early," the demand for a definition is justified. Recognition is early when the cancer is discovered in a stage where it is eradicable – *completely* eradicable, to effect a cure, or *partially,* so that the patient's span of life may be lengthened materially.

There are, of course, some cancers which do not

produce a leading symptom until too late for successful therapy. Others are so malignant that a diagnosis made soon after the appearance of the first symptom—early—is still of no avail. Such exceptional cases would seem to make the definition untenable, but for practical purposes and the usual run of cases, the definition is workable. Successful treatment remains the principal indicator of early recognition which need not be concerned with histologic classification or grading of the tumor.

Statistical Review

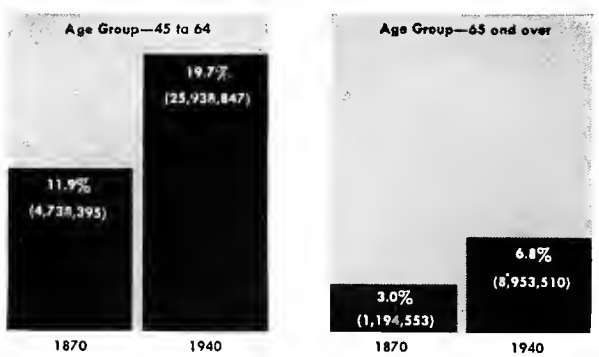
All of us are only too familiar with the sufferings of the cancer patient and the ordeals imposed upon his family. But the full import of the ravages of cancer in this nation and the world over is best shown by the use of statistics.

Cancer incidence and cancer mortality are definitely on the increase. There are those who believe this increase to be actual, while others believe it to be only apparent because of improved diagnostic methods and the increase in longevity. But regardless of the view one may entertain, the positive facts are that more and more people are dying from cancer and many could have been saved by earlier recognition.

Let us examine the charts. Chart I shows the influence of the nation's changed age structure—increased longevity—upon the incidence of cancer.

CHART I

Increasing Numbers Are Reaching the Cancer-Susceptible Years*



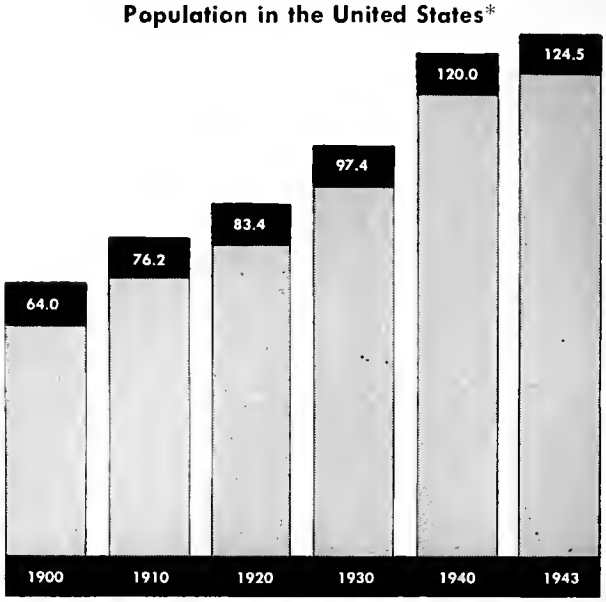
*Comparative figures, for 1870 and 1940, of persons in U.S. in two age groups above 44. Figures indicate percentage of total population, as well as the actual numbers, reaching these age groups. (Selected from Problems of Aging, 2nd ed., edited by E. V. Cowdry, Baltimore, Md., The Williams and Wilkins Co., 1942, and Revised Census of Southern States for 1870 and Statistical Abstract of the United States, U.S. Dept. of Commerce, Bur. of the Census, 1943, p. 5.)

The shaded portions in the left half of the chart indicate the percentages of our population (the actual numbers are also given) who reached the age group of 45 to 64, in 1870 and in 1940. The shaded portions in the right half of the chart show the same for the age group of 65 and over. A comparison shows that the *percentage* of persons who reached these age groups in 1940 was considerably higher than in 1870—a distinct increase in longevity. If we consider these age groups—above 44—as the principal cancer-susceptible groups, it is obvious that the higher incidence of cancer today is accounted for, in part, by the increase in longevity plus the actual increase in population; there are now many more persons in the cancer-susceptible years. But that is not the whole story.

Chart II gives figures on the number of cancer deaths per 100,000 population, since 1900, in the United States. The actual ratio increase is appalling, rising from 64 per 100,000 in 1900 to 124.5 per 100,000 in 1943—almost doubled in 43 years!

CHART II

Cancer Death Rates per 100,000 Estimated Population in the United States*



*Vital Statistics of the U. S., 1943, Part I, p. 14. Figures for 1943 exclude the armed forces overseas.

The steadily increasing destructiveness of cancer is even more graphically illustrated in Chart III, which shows the relative positions of the six leading death-dealing diseases in 1900 and 1943. In 1900, cancer was in last position; in 1943, it had climbed to the position of life enemy No. 2, yielding only to heart disease as a killer of men.

Note that tuberculosis, in the same span, dropped from first place to last, substantiating the value of organized campaigning against an erstwhile malignant disease, and of eternal vigilance on the part of an enlightened population and the medical profession.

While the over-all mortality from cancer has greatly increased, an interesting side light on the trend has been thrown by Mary Grover, in *Public Health Bulletin No. 248*. Breaking down the recorded cancer mortality figures for the years 1900 to 1935, she shows that the *rate* of increase for the female sex has been significantly lower – in each decade—than for the male.

intestinal tract, and bladder. The absence of shaded columns here indicates that these cancers are hopeless when recognized late, but even they are curable in at least 30 to 40% of cases, possibly up to 80%, when recognized and treated early. In the other indicated carcinomatous sites, the potential cures range from 70 to 95%.

This is the challenge. Such an outlook should inspire us to closer scrutiny of our patients, particularly those in the recognized cancer-susceptible age. It should destroy pessimism and defeatism, create hope and confidence. Translated into figures, on the very conservative estimate of 20% of cancer deaths being definitely preventable, it tells us that **we can prevent at least 35,000 deaths from cancer—each year—in the United States alone,** merely by utilizing methods readily available to *all* of us.

It means also that 3,000,000 of our present contemporaries can be spared the miseries of cancer during life, and eventual death through its depredation. A challenge, indeed! It is up to us to meet it.

CONCERNING PATHOLOGY OF CANCER

The physician need remember only a few essential facts about cancer pathology. The essence of cancer is progressive growth, without self-termination, which inevitably ends in death unless checked by surgical extirpation or by irradiation. Cancer exerts its destructive effects through abnormal growth and the progressive-regressive changes which accompany its development.

No cancer toxin or metabolite has been found, which could be held responsible for the deadly destruction brought about by malignant neoplasms and their metastases.

Classification of the Tumor

Differential diagnosis of cancer, on the basis of histologic classification, is not of primary concern to the practicing physician; his interest is in the clinical manifestations which enable him to discover and treat the disease.

Sufficient unto the practitioner is classification according to the organ involved, because the site of the tumor, rather than its histologic structure, determines the clinical picture, the course of the invasion, and the mode of treatment.

The physical reaction of the patient to malignant disease must be distinguished from the behavior of the disease itself. The behavior of the tumor depends largely upon the tissue of origin—connective tissue, muscle, elements of the nervous system, endothelium, epithelium, or some complex tissue.

The pathologist may well look upon cancer of the breast and cancer of the pancreas as the same disease, which it is from the pathologic standpoint. Not so to the clinician, however. He must maintain his independence from purely morphologic viewpoints, and think in terms of treatment for eradication and cure. **Histologically different neoplasms may produce identical symptoms in the same organ, whereas new growths of identical histologic structure may produce entirely different symptoms when located in different organs.**

GENERAL EFFECTS OF CANCER

Some of the effects produced by tumors depend upon features of their growth and development, which are common to all tumors:

(1) Expansive growth produces symptoms of tissue displacement (as in myoma uteri) or of compression (as in the brain).

(2) Infiltrative growth, within the lumina of blood and lymph vessels, will interfere with local blood and lymph circulation.

(3) Tumors located on skin or mucous surfaces tend to ulcerate and become infected, leading to hemorrhage and absorption of toxins.

(4) Regressive changes are not infrequent in tumor cells. When this process is marked, and exceeds the rate of tumor growth, it may well simulate a cure.

Unless the invasion is very rapid, tumor growth produces distinct inflammatory reactions, with all the characteristic signs, in the invaded and surrounding tissues.

Although the principal action of tumors is destructive, certain types retain, at least in part, the functional activities of the tissue of origin; in rare instances functional hyperactivity of the invaded tissue may be exhibited initially. This is notably evident in tumors of the sexual glands.

Course and Rate of Tumor Growth

The course and rate of cancerous growth is not consistent. Progress does not necessarily continue uninterruptedly or at an accelerating rate. Periods of rapid advance may be interrupted by periods of rest or retarded growth.

Pregnancy generally accelerates tumor growth, while the menopause retards it.

Tumor growth may be influenced by the state of nutrition, much the same as this state influences the body in general. There are undoubtedly many other factors influencing the rate of tumor growth, of which we are not aware.

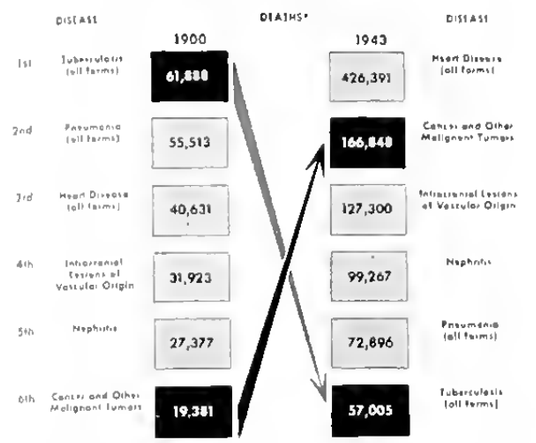
Systemic Effects of Cancer

The visible and palpable changes produced by malignant tumors will be dealt with in subsequent articles, concerned with examination and diagnosis of cancer in specific organs or areas. This section will consider only some of the early systemic effects encountered.

Emaciation—The outstanding systemic change encountered in cancer is emaciation. It must not be considered as always being a late symptom, indicating a hopeless condition; it may be manifest in a very early stage, and may be caused by a

CHART III

The Elevation in Rank of Cancer as a Death-Dealing Disease



*Number of deaths from six leading diseases, in 1900 and 1943, in U.S., arranged in order of decreasing incidence. [Figures for 1900: Mortality Statistics Special Report, 1900 to 1904, p. 76. Figures for 1943: Vital Statistics of the U. S., 1943, Part I, p. 291.]

This finding is substantiated by Table I, which shows that the *rate* of increase for the male has been considerably higher than for the female, although the actual female death rate from cancer has been consistently higher than the male.

TABLE I*

Cancer Death Rates, by Sex, per 100,000 Estimated Population of the United States

Sex	1900	1910	1920	1930	1940†
Male	47.1	59.0	69.6	86.5	114.1
Female	80.9	94.5	97.7	108.6	126.4

*From: Vital Statistics Special Report, Vol. 16, No. 13:53 (July 31) 1942.
† Based on enumerated population.

Table II shows the distribution of cancer deaths in age groups from infancy to old age. This table shows the same trend as the foregoing statistics: an increasing death rate from cancer in *every* age group. It also shows the tremendous jump in cancer mortality after the age of 45. Thus the forty-fifth year marks the beginning of the dangerous age.

The last two columns, carrying the figures of actual deaths in one year (1940) in the United States and in Illinois, bear out the other part of the table in showing that the blight of cancer becomes increasingly menacing from the fifth decade on, and that the state of Illinois is no better off than the rest of the country in that respect.

A Prediction

The foregoing charts and tables show the magnitude of the cancer problem. Unless the situation is promptly improved, it is quite reasonable to make this doleful prediction: During 1946, approximately 165,000 persons are doomed to die of cancer in the United States alone; also: Of all the people living in the United States today, 17,000,000 will eventually succumb to this disease.

TABLE II

Distribution of Cancer Deaths in Age Groups

Age Specific Death Rates per 100,000 Estimated Population in the United States*						Number of Deaths from All Forms of Cancer	
Age	1900	1910	1920	1930	1940	United States† 1940	Illinois‡ 1940
Under 1 yr.	3.2	3.1	3.2	3.1	4.4	89	5
1-4 yr.	2.9	3.3	3.1	4.1	4.8	405	24
5-14 yr.	1.8	1.5	1.6	2.0	3.0	667	36
15-24 yr.	3.2	3.5	3.8	4.2	5.4	1,287	72
25-34 yr.	14.0	14.1	14.7	16.7	17.3	3,696	1,046
35-44 yr.	52.5	55.6	56.0	58.9	61.1	11,198	
45-54 yr.	139.1	156.7	155.1	159.6	168.8	26,180	4,934
55-64 yr.	260.9	322.4	341.2	355.6	369.6	39,071	
65-74 yr.	421.0	541.7	607.7	677.1	695.2	44,328	5,258
75 yrs. and over	555.4	758.4	916.4	1,044.8	1,183.4	31,279	

*From Vital Statistics Special Reports, Vol. 16, No. 13:53 (July 31) 1942.
†From Vital Statistics Special Reports, Vol. 16, No. 13:56 (July 31) 1942.
‡From Vital Statistics Special Reports, Vol. 16, No. 13:55 (July 31) 1942.

Not a pleasant picture, is it? It is predicated on the assumption that no real progress in diagnosis and treatment will be made, and that the present attitude of the public and the medical profession remains unchanged. These factors are the variables upon which we must concentrate and which we must change for the better, if we wish to arrest the anticipated ravages of cancer.

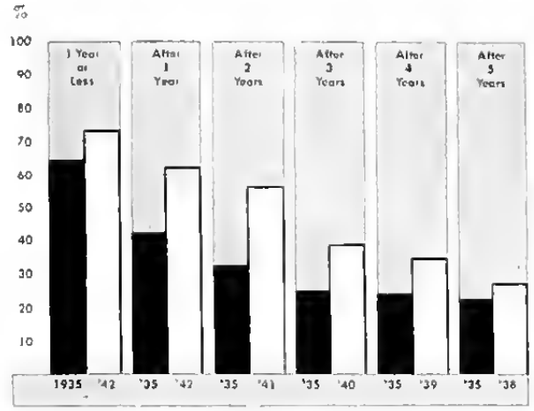
RESULTS OF EARLY DIAGNOSIS AND TREATMENT

Not many years ago, cancer of the stomach was considered hopeless, and no effort was made to eradicate it when found. Today, about 60% of patients with gastric cancer, who seek medical aid, are alive five years after competent surgery. However, in a more limited classification—when the diagnosis is made early enough to permit gastric resection—about 25% will be alive 5 years after operation, and 20% after 10 years. For practical purposes, the latter group of 20% may be considered cured.

Why this discrepancy of 5% in a group of cases, all of whom had the benefit of early diagnosis? Perhaps the following figures will explain it. In the group analyzed, it was found that the time elapsing between the first recognized symptom (the danger signal) and actual treatment (operation) was

CHART IV

Increasing Percentage of Survivals*



*Modified from Figure 2 of article by Ivy, A. C. Some Important New and Old Information about Cancer, What's New (July-August) 1945.

less than 3 months in only 18%, less than 6 months in 37%, less than one year in 59%, and more than one year in 51%.

In other words, **early diagnosis must be followed by earliest possible treatment,** in order to be optimally successful.

Chart IV gives a further demonstration of the favorable influence of early diagnosis. It records the findings of the *Cancer Record Registry* of the Connecticut State Department of Health. This chart shows the percentage of survivals, following histologic diagnosis and conclusion of treatment, in 1935, as compared with each of the years 1938 to 1942.

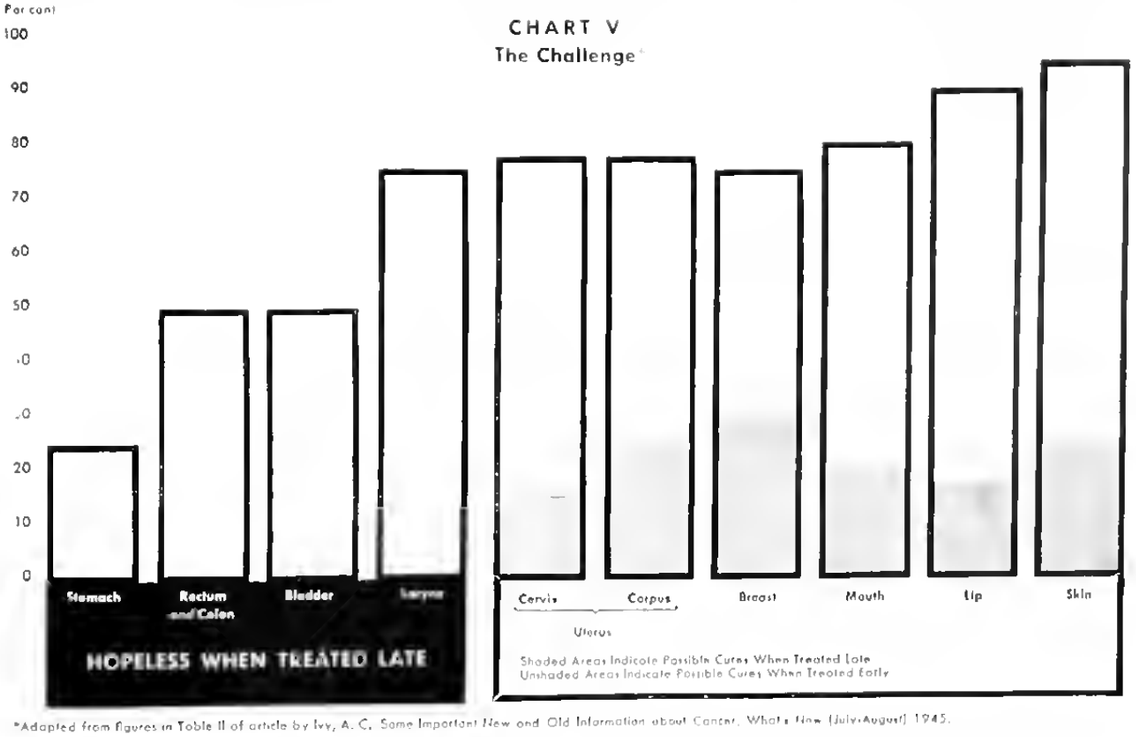
The shaded areas in Chart IV represent the survivals for varying lengths of time—for less than one year, and after 1 year, 2 years, 3 years, 4 years, and 5 years—following diagnosis and treatment in 1935. The unshaded areas show the survivals for corresponding periods in following years, as indicated. It will be noted that the percentage of survivals for the years after 1935—in every bracket—are increased over those for 1935, an encouraging indication of progress.

Up to this point only factual statistical data have been shown. Chart V, however, is intended to serve another purpose. It shows the high percentage of cures considered theoretically possible with our presently available means for early diagnosis and treatment, as against the low percentage of actual cures today. There is a great gap between the two, the factor responsible for this gap is delayed treatment, and delayed treatment is, in the vast majority of cases, due to "too late" diagnosis.

In this chart, the cancer cases are organized according to site, not histologic structure. The first four columns pertain to cancer of the larynx, gastro-

CHART V

The Challenge*



*Adapted from figures in Table II of article by Ivy, A. C. Some Important New and Old Information about Cancer, What's New (July-August) 1945.

relatively benign tumor. Muscular weakness is a conspicuous concomitant symptom.

It is not known whether emaciation is brought about by impairment of metabolism or (most likely) by inanition.

Inanition is not restricted to cancer originating in the alimentary tract; it is present in cancers of other origin as well. It appears to be initiated by a mental depression which engenders aversion to food and loss of muscular tone.

It may not be out of place, in this era of psychosomatic medicine, to mention that the psyche is a delicate indicator of somatic affections, and that otherwise unexplainable personality changes of depressive character may well be the earliest manifestation of serious somatic disease—of cancer, for instance.

Emaciation may be promoted by competition—between body cells and cancer tissues—for the ingested nutriment. Another factor which contributes to emaciation is the actual destruction of body protein, brought about by the febrile condition and bacterial infection which appear to accompany a large number of tumors.

No specific toxic substances have been found in the neoplasm, or in the urine of patients affected.

Anemia—This is a usual, though not invariable, concomitant of cancer. The anemia is generally of a secondary, hypochromic type (except in a group of intestinal cancers).

The principal causes of cancer anemia are: direct loss of blood from macroscopic or microscopic hemorrhage; deficient nutrition; absorption of hemolytic products from necrotic and infected areas.

Leukocytes — Leukocytosis is frequently observed; it results from complications, rather than the malignancy itself.

Erythrocytes — Fragility is normal in the early stages, but usually increases so greatly in the advanced stages that it may even serve as a corroborative diagnostic sign.

Albuminuria — Albuminuria occurs in a high percentage of patients with cancerous emaciation, regardless of the organ involved.

SUMMARY

It is apparent from the foregoing that cancer, in its early stage, does not exhibit any specific or general symptomatic pattern to guide the examining physician toward a correct diagnosis. Pain and functional disturbances — which might arouse suspicion — are only rarely encountered in early cancer. Because of this dearth of early symptoms, it becomes necessary to look carefully into the history of predisposing factors, such as high cancer incidence in the patient's family and occupational exposure to carcinogenic agents.

In the absence of leading symptoms, early diagnosis of cancer will not come from unearthing and running down symptoms related by the patient, but through exhaustive examination of every patient past 40 years of age, who presents himself for any cause.

Cancer therapy is local therapy, whether surgical or by irradiation. So long as this is true, the hope for complete cure rests upon *early diagnosis* and prompt *treatment,* while the tumor is still localized or metastases are not widespread.

But **the fact that remote metastases have taken place, by itself, does not render any case hopeless.** Modern therapy can successfully cope, in many instances, with metastatic processes which a few years ago were considered intractable.

DIAGNOSIS AND STATISTICS

Statistics cannot make a diagnosis, and frequently make laborious reading. The statistical approach in individual physician-patient relationships is valueless, but highly useful in the over-all consideration of diagnostic possibilities. Familiarity with statistical data concerning specific disease incidence may have a profound influence on the physician's diagnostic attitude.

For example, extensive surveys on primary pulmonary neoplasms reveal (1) that an appallingly high percentage of these tumors are inoperable when diagnosed, (2) that one or more warning symptoms or signs were present early in most cases, but (3) these warnings were frequently neglected or overlooked by the patient or the physician. Such knowledge imposes a twofold obligation upon the conscientious physician: Education of the public, and intensification of his own diagnostic efforts.

Chronicity of a symptom always requires thorough investigation. Patients tend to neglect such minor complaints as a mild cough, small discharge, or slight chest discomfort. Hence, when a physician is consulted in regard to a minor ailment involving the respiratory tract, he should urge his patient to report again if all is not well within a few weeks.

The incidence of benign primary pulmonary tumors is insignificant. Most primary neoplasms of the lung are cancerous. If the diagnosis is in doubt, statistics would support the supposition of cancer until proved otherwise.

A Glimpse into Future Issues

In order that you may know what to look forward to in the following BULLETINS, here is a list of subjects we propose to discuss in the next few issues:

(1) Examination of the Patient for Cancer.
(2) Early Diagnosis of Cancer in the Digestive Tract.
(3) Early Diagnosis of Cancer in the Female.
(4) Early Diagnosis of Cancer in the Regions of the Mouth, Neck, and Thorax.

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 2

WHERE DOES THE CANCER PROBLEM LEAD?

In continuation of the statistical data discussed in the preceding number, CANCER BULLETIN No. 1, the reader is referred to the statistical survey shown in Table I of this issue, which supplies a percentage tabulation of the primary sites of cancer, in order of decreasing incidence, as determined by cancer mortality statistics. The combined percentages for organs in related groups are first given, followed by a breakdown of percentages for individual organs in each group, when such figures are significant.

Certain implications from this survey deserve discussion. If the physician's attention is focused largely upon the organs showing the highest incidence of cancer (the digestive organs, uterus, and breast), the likelihood of early discovery and thus of reduced cancer mortality will be excellent, of course. But—

As a corollary, **the less attention is given to the organs showing lower incidence, the greater will be the likelihood of being "too late" in the diagnosis of the less common and rarer forms of cancer.**

The obvious conclusion—the only safe one—is that diagnostic attention must be equally searching on the entire individual, and not too narrowly focused on the parts most likely to be affected.

The physician is concerned with a patient—an individual—not a population. It would be profoundly wrong to let laws of probability, which refer to populations only, influence considerations of differential diagnosis. **The cancer patient's expectancy of survival** does not depend upon the cancer mortality rate but upon the thoroughness and awareness of his examining physician who may well follow the rule running across the top of the pages of each of THE CANCER BULLETINS: In the patient past the age of 40, THINK OF CANCER FIRST; in the patient under 40, THINK OF CANCER, TOO!

A final statistical survey is shown in Figure I, which graphically portrays the percentage figures for frequency of primary carcinomatous sites, separately for the male and the female—a sex-specific tabulation.

TABLE I. CANCER MORTALITY IN TERMS OF ORGANS PRIMARILY AFFECTED

Digestive Organs and Peritoneum	**45.8%**
Stomach	16.2%
Large and small intestines	11.7%
Bile tract and liver	6.3%
Rectum and anus	5.4%
Pancreas	3.5%
Esophagus	1.7%
Other sites	1.0%
Uterus	**10.0%**
Cervix	4.0%
Body	6.0%
Breast	**9.8%**
Respiratory System	**6.7%**
Lung	5.4%
Larynx	0.9%
Other sites	0.4%
Male Genitalia	**6.0%**
Prostate	5.4%
Other sites	0.6%
Urinary Tract (including unspecified sites)	**4.7%**
Bladder	3.1%
Kidney	1.5%
Buccal Cavity and Pharynx	**3.1%**
Pharynx	1.0%
Tongue	0.7%
Other sites	1.4%
Ovary, Tubes, Vagina, etc.	**2.8%**
Skin (except vulva, scrotum, and lip)	**2.0%**
Brain and Cord	**1.6%**
Miscellaneous or unspecified	**7.5%**

Bold figures indicate combined percentages in organs of related groups. Light face figures indicate broken down figures for individual organs. Figures derived from "U.S. Census, 1942: 163,400 Cancer Deaths."

EXAMINATION OF THE PATIENT FOR CANCER

It is rarely indeed that a patient goes to his physician to be "examined for cancer." That is why the title of this section is worded as it is, and not "Examination of the Cancer Patient."

Most men live by the sanguine slogan that "it may happen to you, but it can't happen to me." This is a propitious attitude, but it has its disadvantages, too. It may lead a patient, suffering from early evidences of cancer, to postpone too long his visit to a physician for advice. Therefore, it devolves upon the physician to think of—even suspect—cancer in *every* patient in the cancer-susceptible years, who seeks his advice for any conceivable complaint.

Let us then review the *general aspects* of a search for cancer. Subsequent articles will take up special procedures for diagnosis when the examination has created a suspicion of cancer in a specific organ.

Family Incidence: Heredity

Cancer heredity is still a moot question. In the human, only a few types of cancer have been demonstrated to be hereditary, but it appears to be well established that **susceptibility to cancer may be transmitted by the chromosomes.**

It should not be disconcerting to the patient to be questioned in some detail about deaths in his family, known or suspected to have been due to cancer. If several members of the patient's consanguineous family have suffered from cancer, it should put the physician on the alert, and he should probe for more details: age when discovered, organ involved, duration of illness, treatment used, etc.

If such curiosity arouses uneasiness in the patient, the physician can honestly tell him that anyone may get cancer but that he (the patient) is fortunate in being forewarned of a particular susceptibility, a benefit denied to those without a family history of cancer. The patient is then advised to have regular check-ups—semiannually—provided the present examination arouses no suspicion.

Predisposing Factors

Certain occupations are carcinogenic hazards. Although rigid control measures have reduced the incidence of cancer in the aniline dye, radium and certain other industries, it should be remembered that tar and tar derivatives are carcinogenic, and may be used in forms and ways heretofore unknown. The same is true for radium. The field of usefulness for radioactive substances is widening; one needs only to think of the recent advances made in the field of atomic energy, in order to visualize the vast unknown to which a door has been opened. Research and industry, in their ever-widening scopes, may quite unknowingly expose man to new and different carcinogenic factors, and it may well be that the fate of many will depend upon the keenness of the medical practitioner. Hence, it is important to ascertain the patient's occupation for as long as ten years back, and the length of stay in each of the occupations listed.

Atrophy of the gastric mucosa apparently predisposes to the development of either benign or malignant neoplasms. When gastric anacidity is found, and the blood picture confirms a diagnosis of pernicious anemia, the physician should not be satisfied until the stomach has been thoroughly explored for cancer as well. Liver therapy will have no effect upon cancer superimposed on an atrophic gastric mucosa.

Lymphogranuloma venereum with anal manifestation appear to create some predisposition to cancer of the rectum.

A relationship between single trauma and cancer has not been definitely confirmed. The role of chronic irritation, inflammation, and other such forms of trauma in the genesis of cancer has, however, been established.

THE PHYSICAL EXAMINATION

A. When the History Is Not Suggestive of Cancer

When the history reveals no complaint suggestive of cancer, the physical examination should be even more thorough than otherwise, because symptomless incipience and development are characteristic of the early course of this insidious disease.

Lymph Nodes—Palpation of **all accessible lymph nodes** is imperative. The submaxillary, cervical, and inguinal glands are frequently enlarged from other causes; their size and consistency should be recorded for comparison and evaluation at a later examination. The glands in the supraclavicular fossae and on the lateral thoracic walls deserve special attention. Figure II shows the location of palpable lymph glands, the organs drained, and thereby their significance in diagnosing cancer.

Oral Cavity—A quick inspection of the oral cavity is not enough. Inspect the teeth (particularly any prosthetic replacement) for rough edges or ill-fitting dental work; also look at the lateral aspects of the tongue. **Cancer, particularly of the tongue, frequently results from long-standing mechanical irritation.** And do not pass too hurriedly over any small insignificant-looking lesion on the lip; it may be an early epithelioma.

The Rectum—The rectum, unfortunately, is *usually* overlooked during a routine physical examination. A glance at the anus is not sufficient; digital

exploration of the rectum should be a part of every examination. Early cancer of the rectum has a good prognosis, and can often be discovered by simple digital palpation. **Omission of this maneuver has been responsible for many deaths.** The finger, during this examination, should also be used to gain an impression of the prostate gland, another common site of primary carcinoma.

The Breasts—Examination of the female breasts will be dealt with in more detail in a subsequent section. The breasts, axillae, lateral chest walls, and supraclavicular fossae should be palpated, *first* with the arms hanging by the sides, and *again* with arms elevated and the hands resting on the head. These maneuvers are first done with the patient seated, and repeated with her lying down.

The Female Genital Organs—The gynecologic examination also will be taken up later. It should be emphasized that mere palpation is not sufficient. **A speculum examination, under a good light, is essential** to expose lacerations of the vulva, appearance of the vaginal wall, erosions, ulcerations, lacerations of the cervix, etc.

The Male Genitalia—The condition of the prostate gland is determined by the rectal finger; the external genitalia are inspected and palpated for size and consistency. A hydrocele may be discovered, not infrequently indicative of a tumor concealed by the hydrops.

Fluoroscopic Examination—A fluoroscopic examination of the chest should note the respiratory movements of the diaphragm. Unilateral retardation, or paralysis, in the absence of other symptoms or adhesions, may be the first and only sign of malignant involvement of the mediastinum.

8. In the Presence of a Tumor

Where a visible or palpable lesion or tumor is found, **differentiation between malignancy and benignity becomes paramount.** The simplest steps in this procedure are to ascertain the tumor's consistency, passive motility, relation to the overlying skin, and the condition of the regional lymph glands. Doughy consistency, free motility, precisely circumscribed borders, and easy movement of the overlying skin over the surface of the tumor suggest benignity, but do not altogether rule out malignancy. Biopsy, when practicable, is the safest method of differentiation.

To return to the lymph glands: **The regional nodes of an organ are not always those in closest proximity.** Normal inguinal lymph glands should not be reassuring when a testicular tumor is found, because the lumbar lymph glands, inaccessible to palpation, are the regional nodes for the testes. Likewise, when a suspicious infiltration of the inguinal glands is noted, the cause may be searched for in vain in the anterior abdominal and genital regions, while cancer in the anorectal vicinity is overlooked, yet lymphatics of the anorectal region drain into the inguinal network.

BIOPSY

There are two types of biopsy: routine and rapid frozen section. The latter method is used to establish immediate diagnosis, with the patient on the operating table, and further surgical procedure dependent upon the pathologist's report.

Evaluation—Histologic examination of a small piece of tissue removed from the suspected area is **the most certain method for differentiating a benign tumor from a malignant one.** The pathologist's report of type and grade, when malignancy is verified, is helpful in choosing the method of treatment.

The pathologist usually reports positive malignancy findings by grading the tumor I, II, III, or IV. What significance should be attributed to this classification?

To the patient's physician, cancer is a disease; to the pathologist, it is one aspect of a specifically classified disease type. The pathologist's report must be looked upon as tremendously important—he has pronounced the tumor malignant!—but, even with the grading, does not present the whole picture.

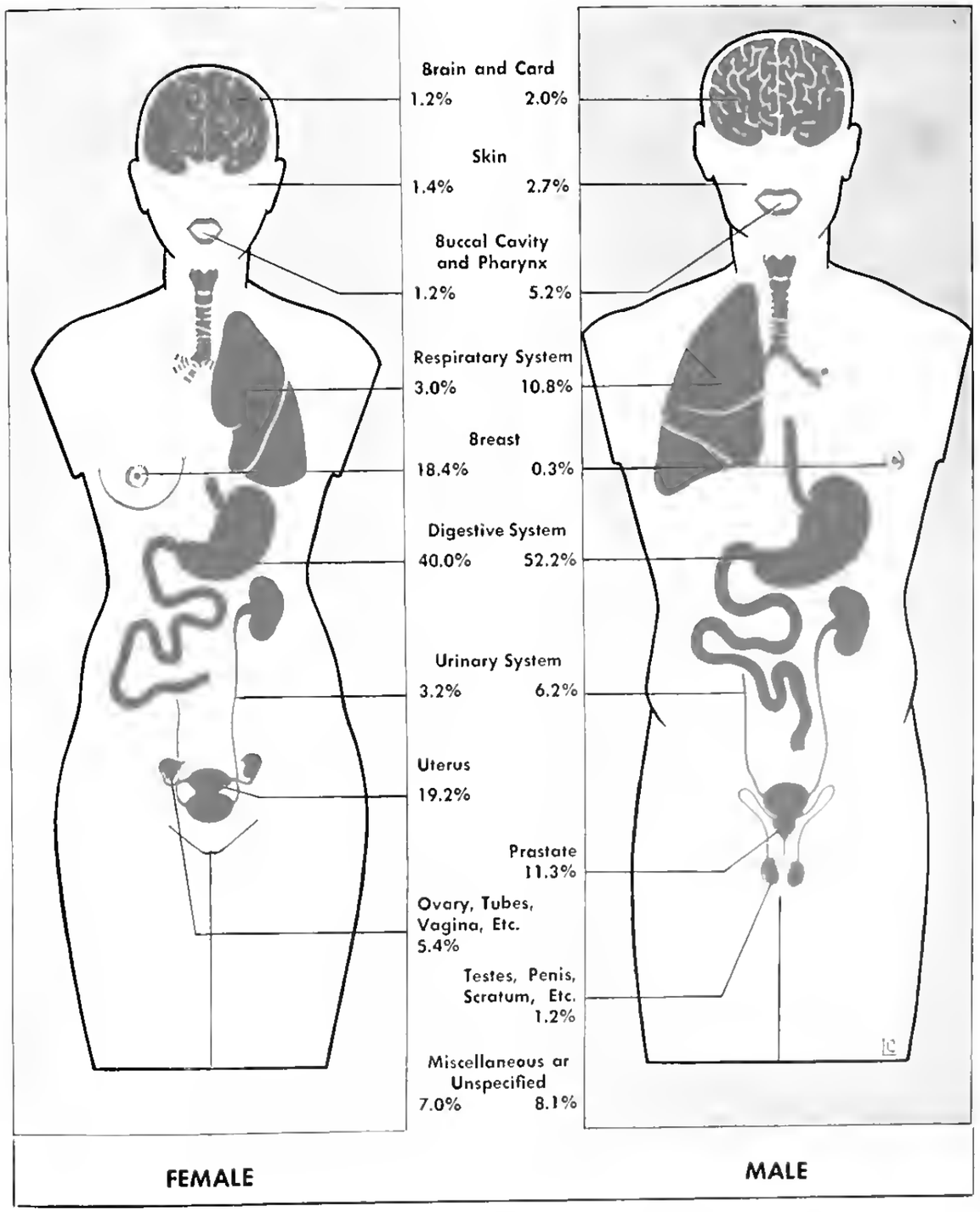
The histologic findings indicate primarily the **potential malignancy** of the neoplasm. This potential must be distinguished from the prognosis of the disease, which depends upon many factors: site of the tumor, extent of metastases, duration of the disease, its recent course, age and general condition of the patient, and perhaps other findings.

Specifically, **the grading of potential malignancy of a neoplasm does not determine prognosis; it is only suggestive,** and to be taken into consideration when weighing all the known factors. In a general way, depending upon the location and the type of tumor, Grades I and II suggest surgical therapy as the preferable procedure, while Grades III and IV suggest radiation. In any case, **when malignancy has been confirmed histologically, speedy action is imperative;** courage, not defeatism, and a sense of responsibility for prompt and adequate action should then guide the conduct of the case; and specialists should be consulted in order to give the patient the best possible chance for a cure.

When **pathologic effusions,** such as appear in the pleural and abdominal cavities, are suspected of having carcinomatous origin, they should be examined. Whether bloody or serous, a microscopic examination should be included because cancer cells may be found free in the fluid, thus clinching the diagnosis.

Methods—Excision by scalpel or cautery knife are the only recommended methods. Undue pressure

FIGURE 1. Sex-Specific Cancer Mortality in 1942, Showing Percentage Frequency of Primary Sites in Each Sex.



PALPABLE LYMPH GLANDS and AFFECTED ORGANS

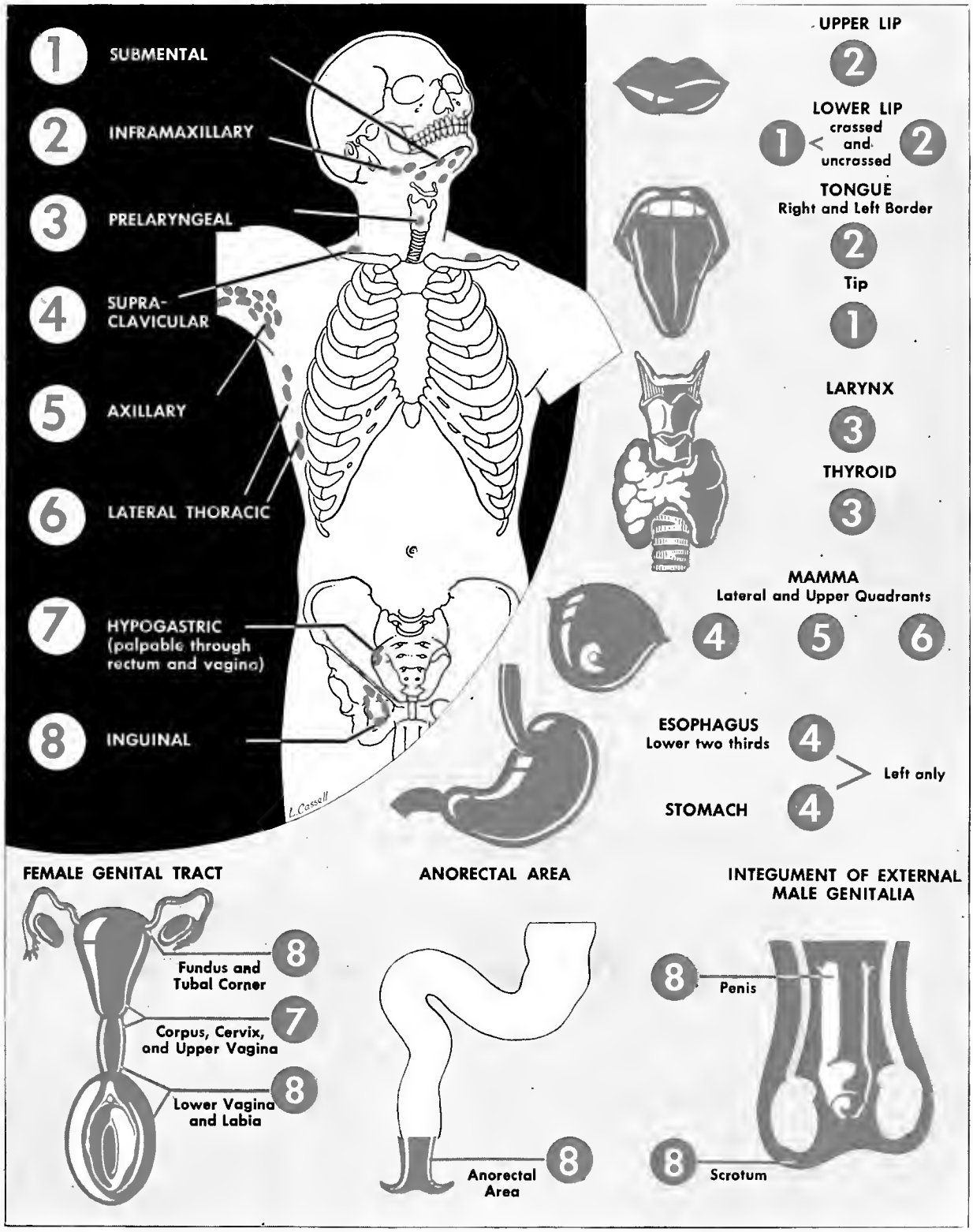


FIGURE II. The anatomic figure shows location and names of all palpable lymph glands which are of importance in the diagnosis of cancer. Each group of glands is assigned a number—1 to 8. The balance of the drawing shows individual organs. The numbers opposite each organ indicate, by comparing these numbers with those of the anatomic drawing, the palpable glands which drain these organs.

on the specimen should be avoided. The specimen should be transferred immediately into a 10% formalin solution, or into Zenker's fluid. (Formalin is a 40% solution of gaseous formaldehyde in saline or water. Zenker's fluid is a solution of mercuric chloride, potassium bichromate, and sodium sulfate in water.)

Securing a Specimen—The completeness and accuracy of the pathologist's report will depend upon how representative the specimen is. The best specimen **for routine biopsy** is one taken near the border of the tumor, including both tumor substance and adjacent tissue. Such a specimen will provide important information as to the reaction of adjacent tissue to the cancerous growth, and will exclude the necrotic tissue usually found in the central portion of the neoplasm. It will also show the relationship between the tumor and the supporting vascular tissue. **In frozen sections,** the best specimen is one taken from the most representative part of the tumor.

Limitations to Preliminary Biopsy—Biopsy before operation is not always advisable. Skin and breast tumors less than 2 cm. in diameter, and melanotic warts should be excised in toto and then examined. Preliminary biopsy of tumors of the testes and of the tonsils is not safe. In neoplasms of the cervix uteri, when necessary to substantiate the diagnosis, it is frequently advisable to irradiate the tumor a few times before cutting into it. Biopsy of a breast tumor should be done only with the patient in the operating room, surgically prepared for immediate radical mastectomy, in case the specimen is found to be cancerous.

When Biopsy Is Negative—The pathologist's report may be negative for cancer, but that does not necessarily mean that the tumor is not cancerous. The specimen taken may not have been representative. Therefore, even when the biopsy report is negative, **increased vigilance is called for,** with regular and close observation of the patient at short intervals until the status of the condition is determined with certainty.

Prompt Action—A routine pathologic report on a submitted specimen should rarely take more than 48 hours—at most 72 hours. Frozen specimens, of course, can be examined and reported on in a few minutes. The latter method is used when the patient is in the operating room, and the surgeon awaits the pathologist's report before determining the exact surgical procedure.

Speedy confirmation of diagnosis is valueless, however, unless followed up by prompt and definitive action. If you are called to see a patient bleeding profusely from a wrist wound, you may recognize immediately that the radial artery has been severed, but the patient will die unless you do something about it **at once.** Just so it is with cancer, too. When cancer is recognized, do something about it immediately—**right now.**

There is another reason for quick action after biopsy: In spite of any assertion or opinion to the contrary, it is not certain that biopsy will not activate tumor growth or encourage metastatic spread. These risks can be minimized by avoiding roughness when palpating tumors and regional lymph nodes, by gentleness in technic when performing biopsy, and by immediate treatment—surgical or radiologic—after confirmation of the diagnosis.

Infection Following Biopsy—Many tumors are infected. Therefore, in biopsy, the risk of spreading infection is greater than in most minor surgical procedures. For that reason it may be well to use antibacterial agents, topically and systemically, for prophylactic purposes.

Choice of Treatment in Cancer

There are at present only two effective modes of treatment in cancer—surgery and irradiation. Which to select and how to apply the selected therapy pose a serious question in most instances. There is only one rule that is generally applicable: In skin cancer, irradiation is usually preferable for cosmetic reasons, even though the curative results may be no better than with surgery.

The average medical practitioner does not see and treat enough cancer to be highly competent in selection or application of cancer therapy. This is no reflection on his ability; it only means that **cancer is best treated by a surgeon or radiotherapist who is highly experienced in the field of cancer.** Every cancer patient deserves the best; anything short of this may prove ineffective or transitory.

Hence it is recommended that consultation be employed to determine the mode of treatment as practiced in approved cancer clinics. This will require that the patient be referred to an experienced cancer therapist, unless the attending physician himself is such a specialist.

Despair Not Called for

It is no longer necessary to consider cancer hopeless because metastases have taken place in distant places, such as the bones. Instead of despairing, consult a radiotherapist. Cure may not be possible, it is true; but years may be added to the patient's life—years of usefulness and freedom from distress. Let it also be remembered that in some cases, even with distant metastases, **eradication of the cancer may yet be possible.**

●

BULLETIN No. 3—the issue soon to follow—will present: "Early Diagnosis of Cancer in the Digestive Tract."

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. 1 NO. 3

EARLY DIAGNOSIS OF CANCER IN THE DIGESTIVE TRACT

Up to this point, THE CANCER BULLETINS have been chiefly concerned with a rather general discussion of the cancer problem.

A statistical survey has shown how ravaging cancer really is: the multitude it cuts down each year, the misery and havoc it causes in family and economic life.

The high lights of information which should lead to suspicion and early diagnosis of cancer *anywhere* in the body have been presented.

It now becomes the purpose of the BULLETIN to consider cancer of specific organs and to review the symptomatology and diagnostic methods for the detection of this predatory enemy in its nonage before it has passed the age of restraint.

Refer back, for a moment, to Table I in BULLETIN No. 2, and you will note that **mortality is higher—45.8% in 1942—in cancer of the digestive tract and peritoneum than in any other group of related organs.** Refer also to Chart V in BULLETIN No. 1, and it will be seen that cancer of the stomach, rectum, and colon are **hopeless when treated late.** Hence, *early* diagnosis is of the gravest import in cancer at these sites and constitutes a highly critical part of our defense.

THE ESOPHAGUS

Esophageal cancer is highly malignant and difficult to diagnose, except in the later stages. Hence, its **mortality figures are out of proportion to its incidence,** as compared with cancer in some other organs. For the past twelve years, more than 2,000 persons have died each year from carcinoma of the esophagus.

The majority of esophageal malignancies are diagnosed between the ages of 40 and 50 years. It is found five times as often in men as in women.

Metastases to the regional lymph glands occur early—often before symptoms induce the patient to see a physician. For this reason **early diagnosis is seldom made except by the alert physician who recognizes it as an incidental finding during an examination for other cause.** Unfortunately the lymphatic channels of the esophagus drain into nodes which are inaccessible to palpation, except that a part of those supplying the upper two thirds drain into the *left* supraclaviculars. Therefore, **enlarged left supraclavicular nodes should make the examiner think of the esophagus as a seat of malignant growth.**

It is also unfortunately true that the present modes of therapy for esophageal cancer are so unsatisfactory that **the only chance for cure lies in very early recognition.** There are indications, however, that new surgical and radiotherapeutic approaches may improve this unhappy situation in the near future.

Symptomatology

The first phase of esophageal cancer is *silent.* The disease has definitely progressed before symptoms become manifest.

Dysphagia—One of the earliest as well as most significant symptoms is dysphagia, a symptom more often associated with cancer of the esophagus than with any other condition. **Dysphagia coexisting with hoarseness is practically pathognomonic.**

Although the obstructive process results from a slowly progressive neoplastic growth, the first evidence of dysphagia frequently is an acute and dramatic incident connected with rapid eating of a solid food. Unfortunately for the patient, too often he overcomes the momentary difficulty by drinking plenty of water and, frightening though the incident may have been, he fails to consult a physician; instead, he tries to avoid recurrences by more careful eating. In the meantime, tumor growth continues and metastasis progresses; only after a fatal delay will the recurrences of obstruction become so serious that a physician is consulted.

Because of this biphasic course of dysphagia, which too often leads to fatal delay, it becomes most important, when examining a patient over 40 years of age for any reason, to ask these questions:

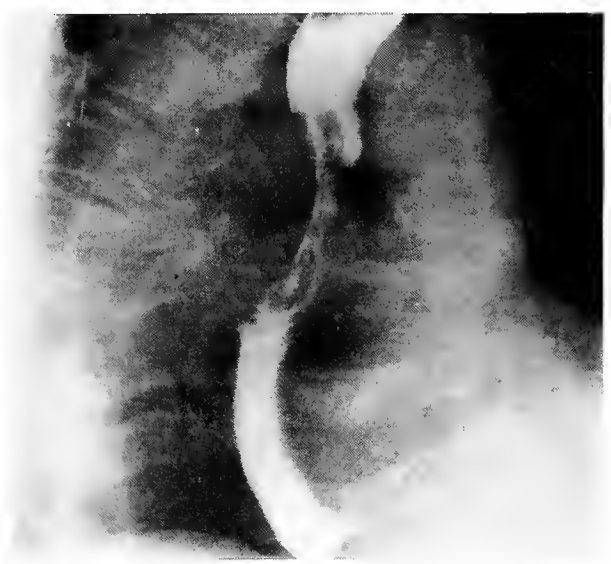
"Did you ever experience difficulty in swallowing your food?"

"If so, under what conditions did it occur?"

"What happened thereafter?"

When there is even a mention of a past dysphagic incident by a patient, no matter how slight the difficulty may have been, investigation should brook no delay. It must be ascertained at once whether the condition was of functional or mechanical origin. In this connection, **an important point to remember** is this: A physician who uses fluoroscopy for examination should not administer barium for such an examination, unless he is capable of following through with a competent radiologic exploration of the gastrointestinal tract; his examination should be restricted to checking of the mediastinal shadow and diaphragmatic movement. The reason for this is: If crypts or fossae are encountered, they will fill with barium, and it will be necessary to postpone referring the patient to a radiologist until the crypts or fossae are emptied of their barium—an unwarranted delay.

FIG. 1
Roentgenologic Diagnosis



Esophageal Carcinoma—Only small ribbons of barium pass the tumor mass which protrudes into the esophagus. Dilatation of the esophagus above the incomplete obstruction not marked as yet.
(By courtesy of Northwestern Univ. Med. School X-Roy Dept.)

Even though x-ray findings are negative, a patient giving a history of dysphagia should be kept under close observation. If the x-ray findings arouse suspicion of a cancerous origin, or if the attacks of dysphagia recur even without suspicious findings, esophagoscopy is imperative.

In spite of obstruction, actual regurgitation of food occurs less commonly than might be expected. When there is regurgitation, the vomitus should be examined to determine whether any digestion of food has taken place, and for presence or absence of hydrochloric acid. If the vomiting takes place one or two hours after eating and is of gastric origin, some degree of digestion will be found and the vomitus will show an acid reaction.

Pain—Pain may be an early symptom—earlier even than dysphagia—but ordinarily is a later finding. It is not related to the dysphagia, although it may accompany it. The pain is felt over the anterior thoracic midline, corresponding to the site of the tumor, and is of a heartburn, not colicky, character.

A major factor in the elicitation of pain (heartburn or pyrosis) seems to be distention of the esophagus. It is not caused by regurgitation of acid gastric juice into the esophagus; it has even been observed in the presence of complete anacidity. Hence, **when heartburn is a persistent and prominent complaint, think of malignancy in the esophagus or stomach.**

Physical Signs—If there is a depot of stagnant food above an obstruction in the esophagus, it can be detected by percussion of the thoracic vertebral area; the sound above the stricture will be dull. In the presence of a stricture, with dilatation above it, an area dull to percussion may be created by drinking one or two glasses of water. This is a useful procedure when there is no stagnant food present or the percussion dullness is not distinct.

The presence of a hard, hypertrophied *left* supraclavicular lymph node is significant.

THE STOMACH

When we consider carcinoma of the stomach we are dealing with **the outstanding mortality producer of the entire cancer group:** About 25,000 persons die every year in the United States from cancer of the stomach.

The fifth and sixth decades (40 to 60 years of age) are the ages of highest incidence, but it must be remembered that gastric cancer does occasionally occur even before the age of twenty.

Patients are prone to delay consulting a physician in regard to manifestations of this disease. It is estimated that the average person waits approximately six months after the initial symptom before he seeks relief. A further delay of several months is usual before the diagnosis of cancer is established. As a result, **it has been estimated that the total time elapsing between the appearance of the first symptom and the established diagnosis of cancer usually amounts to about a year.** This unwarranted delay, induced by neglect on the part of both patient and physician, is definitely and greatly reducible.

To make matters worse, it is also true that more than 50% of all gastric cancers metastasize even before the initial symptoms appear. Add these two factors together—presymptom metastasis and unwarranted delay in reporting of symptoms—and it becomes obvious that the chances of making an early diagnosis are poor indeed if we depend for diagnosis upon symptom manifestation rather than thoroughness and acuity in routine physical check-ups in the cancer-potential years.

FIG. 2
Roentgenologic Diagnosis

Gastric Carcinoma—Showing a malignant neoplasm extending along the greater curvature (between arrows).
(By courtesy of Dr. F. L. Husse, Northwestern Univ. Med. School X Ray Dept.)

Gastric Sites for Cancer—Malignant neoplasms show definite predilections in their choice of sites for primary invasion in the stomach. The lesser curvature, at the antrum and near the pylorus, is primarily invaded in about 72% of all cases; diffuse involvement of the entire stomach occurs in about 15% of the remaining 13%, most begin in the fundus, with a few along the greater curvature.

The site of origin has diagnostic implications, because the appearance of symptoms depends greatly upon the part involved. Tumors along the greater curvature and in the fundus (13%) remain long silent, while those near the pylorus tend to impair gastric motility and emptying, even in the early stage, thereby producing early symptoms.

The site also has an important bearing on lymphatic drainage, gastric chemistry, and metastases. Cancers located on the greater curvature and in the upper half of the fundus metastasize much later than those located at other sites, because of the paucity of lymph vessels in these areas. Tumors at the cardia or the pylorus metastasize early.

Significance of Gastric Acidity—Lowered gastric acidity is an important, though somewhat overrated, symptom in cancer of the stomach. The degree varies with the cancer site.

In cancer of the pyloric region, particularly when the mucosa is ulcerated, hyperacidity is usual. It simulates simple peptic ulcer in so many of its manifestations that it may easily be mistaken for an ulcer: hyperacidity, severe pain, pylorospasm, and temporarily favorable reaction to peptic ulcer therapy frequently lead to faulty diagnosis. There may even be a weight gain under peptic ulcer therapy while the tumor is progressing.

It is quite possible that hypo-acidity and anacidity do not result from malignancy, but that an already established achylia prepares the ground for cancerous degeneration, a particularly plausible postulate in cancer of the lesser curvature. The anacidity may have resulted from chronic gastritis preceding the new growth. Therefore, any patient who is known to have hypo-acidity should be carefully checked every few months, even in the absence of subjective gastric symptoms.

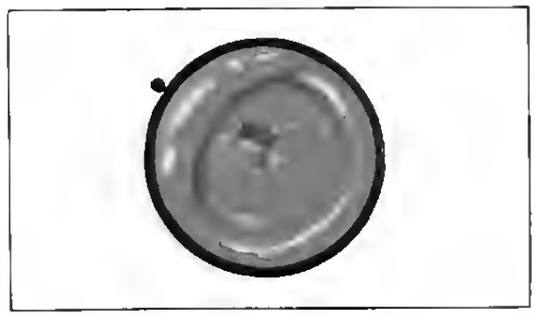
Symptomatology—During any examination, even though the patient makes no complaint of epigastric discomfort, he should be asked if he has had any belching, vague feeling of fullness, or increased sensitivity to slight overeating and to deviations from the customary diet. He may have had mild symptoms, relieved by voluntary reduction and restriction in eating, and fail to report them.

Aversion to rich food and to meat is a frequent symptom, and may divert the physician's attention to the hepatobiliary tract.

Decreasing appetite is usually one of the first symptoms complained of. **Anorexia and nausea,** in a patient previously untroubled by alimentary difficulties, should always be given serious consideration; think of beginning pyloric obstruction.

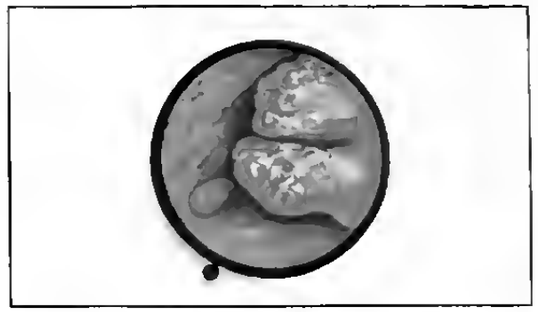
Mention has already been made of the danger of confusing the early symptoms of cancer in the pyloric region with peptic ulcer, because of hyperacidity and improvement under ulcer therapy. Hence it should become routine practice to **have competent roentgenologic examinations made in all peptic ulcer cases,** and not to rely entirely upon office examination and laboratory analysis of the gastric contents. Even though no suspicion of cancer is aroused by one such examination, it is advisable to have it repeated in four to six weeks, preferably by the same radiologist who is in a better position for comparative evaluation, and who knows the

FIG. 3
Gastroscopic Diagnosis



Gastric Carcinoma—A small ulcer visible within the irregularly shaped pylorus, diagnosed as carcinoma. Diagnosis histologically confirmed. (By courtesy of Dr. Rudolph Schindler, Los Angeles, Cal. From Surg., Gynec.& Obst. 69:1 (July) 1939.)

FIG. 4a
Gastroscopic Diagnosis



Gastric Carcinoma—On posterior wall, near greater curvature, upper half of stomach. Diagnosis histologically confirmed.
(By courtesy of Dr. Rudolph Schindler, Los Angeles, Cal. From Surg., Gynec.& Obst. 69:1 (July) 1939.)

amount of x-ray exposure the patient has been subjected to (a precaution against x-ray burns).

A **chronic dyspeptic,** a complainer of long standing, can and may also develop cancer. Unless his physician is on the alert, such a patient is particularly apt to be a victim of oversight. Cancer will, however, bring about a change in the symptom complex, previously so monotonous and unchanging, and it is up to the physician to discern the change at once.

Hematemesis or **melena** may be the first sign recognized by either patient or physician; it is virtually the only early sign of cancer in the "silent area" of the stomach. X-ray examination and introduction of a gastric tube are inadvisable soon after a massive hematemesis, but examination for occult blood should be the first test done after about a ten-day wait. When positive, malignancy must be considered as a likelihood.

An early symptom of cancer at the cardia may be **dysphagia** which is also a symptom of esophageal cancer. No harm will come from mistakenly suspecting the esophagus, because esophagoscopy will correct the error. Roentgenologic demonstration of cancer of the cardiac area of the stomach is difficult and unreliable, because the principal indication of an early neoplasm—derangement of the mucosal pattern—can rarely be visualized distinctly enough in this part.

Anemia is commonly an associated symptom. **Pallor, loss of weight,** progressive **loss of endurance** call for blood examination. The anemia is usually of the secondary type (hypochromic, microcytic), but in some instances may be of the primary, pernicious type. If, in a patient with anemia and progressive asthenia, x-ray examination fails to show a gastric cancer, further examination of the colon should be made, because **cancer of the colon, in its early stage, may produce similar symptoms.**

Physical Examination A palpable mass may or may not be distinguished in the upper abdomen.

FIG. 4b
Raentgenographic Failure

X-ray film of same stomach as shown in Fig. 4a, made previous to gastroscopic examination and reported normal.
(By courtesy of Dr. Rudolph Schindler, Los Angeles, Cal. From Surg., Gynec.& Obst. 69:1 (July) 1939.)

Its absence should not allay suspicion; even extensive cancerous invasion of the stomach may not be palpable to the examining hand.

A hypertrophied, hard, **supraclavicular lymph node on the left side is highly suspicious** of cancer, but **bilateral palpable supraclavicular nodes speak against cancer of the stomach.**

When palpating the axillary nodes, particular attention should be given to the area below the lateral edge of the pectoralis muscle. If palpable nodes are found in this area on *the left side only,* gastric malignancy is quite likely to be the cause.

Laboratory Examination—Laboratory examination of the feces for blood should be routine. Most cancers ulcerate the mucosa and betray their presence by persistent oozing of blood.

The stomach contents should be examined for evidence of occult blood, but precautions must first be taken to assure the examiner that the patient has been on a diet free from hemoglobin or other matter which might nullify the value of the chemical test for occult blood. On the other hand, only frequently repeated negative tests should be accepted as assuring evidence against malignancy.

The significance of hypochlorhydria and anacidity has been indicated. When the value for free acid is twenty or more units below that of total acid, and when absence of free acid is accompanied by a relatively high total acidity, the stomach contents should be tested for lactic acid also.

The occurrence of **achylia, lactic acid, Boas-Oppler bacilli,** and other symptoms of obstruction

should not be interpreted as indicating a hopelessly advanced case of stomach cancer. These findings **may occur in an early stage** of cancer, as well as in obstruction from other cause.

Diagnosis—In the eyes of the law, a man is considered innocent until and unless proved guilty. In medicine, with reference to cancer diagnosis, the only safe attitude is to assume the presence of cancer until and unless it can be proved that it does not exist. This attitude is particularly relevant in the examination for carcinoma of the stomach because, when symptoms are manifest, the disease, if present, is usually no longer in its early stage. Most important, however, is this: **Think of and look for cancer in every cancer-age patient, before the symptoms are manifest.**

Remember, also, in differentiating the diagnosis of cancer, that prostatic hypertrophy may simulate many of the features of gastric cancer such as vomiting, pallor, anorexia, and loss of weight.

THE COLON

Including the Sigmoid and Rectum

It is estimated that approximately 50,000 persons in this country harbor cancer of the colon or rectum in the presymptomatic stage. **A large percentage of intestinal cancers develop in the sigmoid and rectum,** and of these, 90 to 95% are within easy reach of the examining finger, the rectoscope, or the sigmoidoscope. Only 5 to 10% are difficult to reach. Yet, in spite of this favorable condition for diagnosis, and despite the fact that colonic and rectal cancer tend to be quite advanced before metastasizing, about 10% of all cancer deaths are chargeable to this type of cancer annually.

An average of nine months is said to pass between the onset of symptoms and hospitalization for treatment in most rectal cancers, and twelve months in cancer of the colon. This is a situation which can and must be changed. All that is required is that the physician become more conscious of the **vital importance of routine rectal examination.** A great reduction in cancer mortality will inevitably follow.

Symptoms—Symptoms tend to manifest themselves early in cancer of the large bowel. But they are neither intense nor dramatic, since there are no particularly sensitive areas in this bowel. There are no pathognomonic signs; hence any symptom connected with the colon or rectum should compel consideration of cancer as the possible cause.

The **constitutional symptoms** are dyspepsia, anemia and cachexia, anorexia, loss of weight, asthenia, fever, and leukocytosis.

Important is the history of a change in bowel habits. These are referable to irritation of the colon or peritoneum, ulceration by the new-growth, or mechanical obstruction. Physiologic peculiarities of the various portions of the large bowel account for variations in the symptom complexes according to the site of the tumor; certain features of the tumor itself account for similarity of some of the symptoms regardless of site.

Ascending Colon and Right Half of Transverse—The primary function of the ascending and the first part of the transverse colon is to absorb nutrients from the chyme. The liquidity of the contents and the large diameter of the intestinal lumen minimize the possibility of obstruction in the ascending colon. Rather, the symptoms of malignancy in this area arise largely from absorption of toxic material through ulcerated surfaces created by the neoplasm.

The usual symptoms are **anorexia, belching, sensation of fullness, nausea and vomiting, asthenia,** and **loss of weight.** The **temperature** is frequently elevated and, in many instances, there is an intense **anemia,** usually of the hypochromic type, induced by the toxemia rather than by blood loss which usually is slight.

Pain may be present, but it is indefinite and of no help in localizing the tumor. Intense, colicky pain usually indicates obstruction; most often in the hepatic flexure.

Constipation or diarrhea are only occasionally encountered; even more rare is alternating constipation and diarrhea.

If the mucosa is ulcerated and bleeds, the blood mixes with the liquid chyme, concealing the appearance of visible blood in the feces. **Melena** may occur. Examine the feces for **occult blood** if there is the slightest suspicion of cancer.

Left Half of Transverse Colon, Descending Colon, Sigmoid and Rectum—Traversing this portion of the colon, the intestinal contents gradually lose their liquidity, and change from fluid to semisolid, then to solid fecal matter. This change of consistency, together with the tendency for neoplasms of the descending colon, sigmoid, and rectum to take an **annular** form (encircling the bowel and gradually narrowing its lumen) favors early appearance of symptoms of obstruction, before constitutional symptoms and signs are manifested.

Obstruction takes a slow, progressive course. Therefore, its manifestations are not like those of an ileus, although ileus *may* occur. The first complaints are of indefinite, vague abdominal pain, then griping or colicky pain, increasing difficulty in obtaining a bowel movement, and finally complete inability to have an evacuation.

As in obstructive dysphagia, the patient is prone to take the increasing difficulties too lightly, consider them as evidences of mere constipation, and dose himself regularly with cathartics. Thus keeping the bowel contents liquefied, he is not aware of the seriousness of the situation until the obstruction is complete. In the meantime, he has failed to inform his physician of his trouble. Hence, it is important for the physician, in the course of routine examinations, to **probe carefully into the history**

when mention of diarrhea or constipation is made.

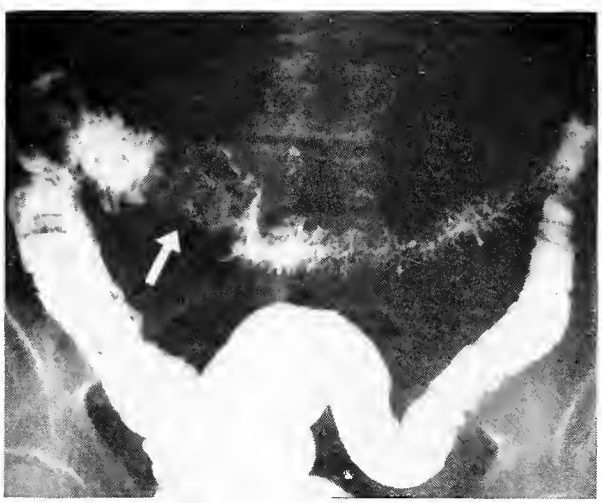
When the tumor has ulcerated, blood and mucus may be grossly discernible in the red or **tar-colored feces. Bleeding**—frank or microscopic—is **one of the earliest and most significant** signs.

Rectum—Cancer of the rectum kills about 9,000 persons every year in the United States.

Of all the divisions of the large bowel, the rectum is the most accessible for examination, hence the easiest to check and spot the beginnings of cancer.

The pressure and friction exerted by solid fecal matter against ulcerations or protrusions of the neoplasm, in the comparatively narrow rectal pathway, lead to early manifestations such as **bleeding and alteration in bowel habits.** The blood from rectal hemorrhage is grossly and readily discernible —and is always a significant sign.

FIG. 5
Roentgenologic Diagnosis



Carcinoma of Transverse Colon—Compare the distorted mucosal pattern in the right half of the transverse colon (arrow points at tumor area) with the fine, rugose pattern in the left half.
(By courtesy of Northwestern Univ. Med. School X-Ray Dept.)

Hemorrhoids are common, and may coexist with cancer of the lower bowel. Hemorrhoids also may bleed, but it is inexcusable to assume that bleeding is of hemorrhoidal origin, merely because hemorrhoids are present. **Bleeding from intestinal cancer is more frequent than from hemorrhoids;** therefore, the real source of the blood must be accurately determined and not be assumed. **Think of cancer first, hemorrhoids later!**

Change of bowel habits—**progressive constipation** is the usual change—is the **most constant early symptom.** Unfortunately, this is too often assumed to be just an indication of growing older and a result of lessened physical activity. Instead of consulting a physician, the patient therefore consults a druggist and takes laxatives or cathartics to overcome the constipation.

In a few cases, there is **diarrhea** instead of constipation, and it behooves the physician who may be consulted for this, to search diligently for the cause, remembering that malignancy in the lower bowel may be the etiologic factor.

Rarest of all is constipation alternating with diarrhea. This sign, and the "ribbon stool" sign, have been too much emphasized in some standard texts. When present, think of cancer, of course. But when absent, do not discount the possibility of cancer because, as mentioned above, these are rare, not common, signs of malignancy.

A rather typical symptom is the **"foreign body" effect** on the defecation reflex. This "foreign body" feeling is exemplified by frequent urges to defecate, without relief from the urge even after defecation is accomplished.

Pain is not an early symptom, but may become prominent as the sphincter becomes involved in the new growth.

Constitutional symptoms, as previously enumerated for cancer elsewhere, are late symptoms, not frequently encountered.

Physical Examination of the Abdomen—Only about one third of the time will a tumor be detectable by abdominal palpation. When felt, the surface of the tumor is nodular, the consistency hard, and the mass may or may not be freely movable. If inflammation is extensive, the mass may be considerably larger than the cancer tumor itself.

Palpability of the tumor is not necessarily a late sign.

Rectal Examination—The value of routine rectal examination cannot be overestimated. **Digital examination is the most important procedure** for determining pressure, fixation, extent, and consistency of a tumor mass, as well as palpation of hypertrophied lymph nodes and extrarectal affections.

It is possible that an area of indurated inflammatory tissue may be mistaken for a malignant infiltration, but such an occasional error is greatly preferable to missing the diagnosis entirely, or to overlooking a cancerous growth.

Proctoscopy and sigmoidoscopy may now well complete the diagnostic procedure for the lower colon—up to 25 cm. (10 inches) from the anal exit. Visualization is more valuable than the x-ray for this part of the examination.

Roentgenologic examination is, of course, invaluable for diagnosis in the parts of the colon which cannot be visualized. **When obstruction is present or suspected, barium by mouth is contraindicated;** it might cause complete stenosis and require emergency surgery under unfavorable circumstances. The barium enema should be used in these cases.

It may bear repeating here: **The inguinal nodes drain the anorectal area.**

BULLETIN NO. 4, the issue soon to follow, will present "Early Diagnosis of Cancer of the Breast and Female Genital Organs."

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 4

EARLY DIAGNOSIS OF CANCER OF THE BREAST AND FEMALE GENITAL TRACT

Reference to Table I in a previous issue of THE CANCER BULLETIN (Vol. I, No. 2), will reveal that the female breasts and genital tract provided primary sites for more than 20% of fatal cancers in the United States in 1942.

When it is remembered that these sites are among those most accessible to inspection and to examination by direct palpation, it can only be assumed that neglect on the part of the patient or negligence on the part of the physician, or both, must be responsible, to a great extent, for the high mortality rate. Cancer mortality is greatly reducible in cancers originating in these sites, because early diagnosis is feasible; alertness and a suspicious attitude on the part of the examining physician will lead to earlier detection of cancer in a large percentage of cases.

THE FEMALE BREASTS

About one-fifth of all cancers in the female originate in the breast. The accessibility of the breast and its regional lymph nodes, both to examination and treatment, renders the outlook bright for a substantial reduction in cancer mortality due to primary breast involvement.

It was pointed out in Chart V (The Challenge) on page 4 of the first issue of THE CANCER BULLETIN that it is reasonable to expect **75% of cures** in breast cancer **when diagnosis is made early and treatment is prompt.** Even in the highly malignant type occurring in young women, the chances for cure are greatly increased if the diagnosis is made early and adequate treatment is given before metastases appear in the axillary nodes. If treatment is delayed until the skin of the breast or the regional lymph nodes are involved, the odds are against cure: not more than 25% can be expected to survive for five years or more even after radical surgery.

The propensity of the mammary gland for malignant degeneration does not reach its peak until full maturity of the organ. Hence, cancer of the breast rarely occurs in women under 25 years of age. The ages of highest incidence are from 45 to 55, indicating a significant relationship with the transitional period of ovarian function. After the fifth decade, the incidence again decreases.

Clinical experience has furnished evidence of a definite relationship between breast cancer (susceptibility and course) and the generative function. Nulliparous women are more susceptible than the parous, but pregnancy and lactation, engendering maximal mammary activity, render the course of a pre-existing breast cancer much more malignant—a situation not mitigated by interruption of the pregnancy.

A fortunate coincidence exists: The highest percentage of five-year cures is obtained in cancer involving the lateral hemisphere of the mammary gland, which happens also to be the site of highest incidence of cancerous invasion.

Signs and Symptoms

In the early stage, there are few, if any, subjective symptoms. Pain due to inflammatory reaction in adjacent tissues occurs but rarely in this stage.

Pain in the breast indicates a benign lesion more often than a malignant one, but its nature should always be carefully and certainly determined. Pain from cancer tends to be constant; pain from chronic cystic mastitis is intermittent, increasing in severity at the menstrual period and reaching its peak just before the onset of the flow. The inflamed lumps in mastitis usually are much more sensitive to touch and pressure than the lumps of cancer.

Localized pruritus with eczema of one breast may be much more significant than pain. Although this manifestation appears to be a relatively rare one, it should be regarded as a harbinger of cancer in the making, a forerunner of its palpably detectable signs. Hence, every patient complaining of localized

itching of a mammary gland should be closely watched for cancer.

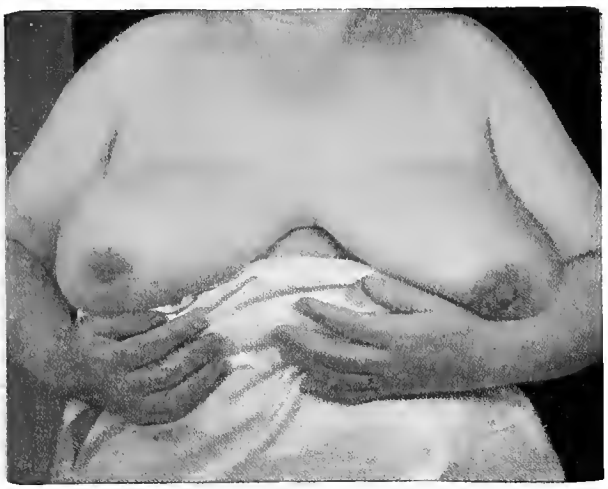
Most breast cancers are discovered through their visible or palpable manifestations—all too often by the patient herself. Inasmuch as many patients refrain from seeking professional advice until the invasion has reached an advanced stage, the physician's great opportunity still remains in accidental discovery during a physical examination for other cause. **That opportunity makes mandatory careful examination of the breasts as an essential part of the routine examination of every female patient over 25 years of age.**

The Examination

The patient should be bared to the waist and examined in various positions: upright, seated, and supine.

Contraction of the chest muscles, by varying the positions of the arms, is a valuable procedure for revealing abnormalities of the breasts, particularly by bilateral comparison. To accomplish this, the patient's arms should first be placed at her sides, then be raised above the head. For relaxation in this position, the hands may be folded on the head, and the upper arm may be supported by an assistant or a high-backed chair. This maneuver should be repeated in the reclining position.

FIGURE 1
Cancer of the Right Breast



Right nipple is retracted. Lateral contour of right breast is straight (almost vertical), in contrast to smooth convexity of lateral contour of left breast.
(Courtesy of *What's New*, March, 1946)

In addition to the breast itself, special attention should be given to the axilla and lateral chest wall, and the supraclavicular fossa. The flat hand and fingertips should be used in palpating the breast; pinching the mammary tissue between the thumb and fingers yields confusing results.

Inspection—The breasts should be carefully inspected for asymmetry of position, enlargement of one, or deviation in form from the normally arc-shaped outline, as indicated by areas of flattening or protrusion. Any of these signs are of pathologic significance. **Localized flattening in the contour of the breast is a particularly suspicious sign, and nearly always the result of cancer;** it may be superficial or deep-seated enough to involve the pectoralis major muscle. Irregularity of contour may be the first apparent manifestation, but it is not an early sign.

The Nipple—Retracted nipples are not rare. They may be found, unilaterally or bilaterally, in otherwise normal breasts. But gradual and progressive retraction and fixation of the nipple are almost invariably pathognomonic signs of an advancing malignant neoplasm. Hence, it is of utmost importance to record the type of nipples found on first examination of every female patient, and to inquire about any possible recent change in nipple type, if retraction or other abnormality is encountered at the first examination.

Retraction may be an early sign, caused by a superficial carcinoma originating in the nipple area; or a late sign, caused by a tumor originating in the periphery or deep central portion of the breast. Absence of nipple retraction does not, however, imply absence of cancerous invasion of the breast even in an advanced stage.

Discharge—Of the four usual types of abnormal nipple secretions—blood, serum, white fluid, or thick greenish fluid—the first three are suggestive of cancer, and necessitate careful examination for its discovery. A bloody discharge is not always cancerous, but it is most fearsome to the patient and most conducive to leading her to consult a physician. For this reason, a bloody secretion leads to discovery of an underlying cancer more often than the less feared non-bloody discharges.

Skin—Intractable eczema affecting the nipple and areola, in women between 40 and 60 years of age, may indicate intramammary cancer, usually an adenocarcinoma. The cutaneous lesion itself represents a secondary epidermal carcinoma (Paget's disease), showing Paget cells (now considered to be cancer cells) on microscopic examination. Usually, some exudation and itching accompanies the eczematous lesion.

Puckering of the skin of the breast is a diagnostic sign of first importance. When not plainly apparent it can be made so by raising the patient's arm to the upright position; or, in women with voluminous breasts, by pushing the breast of the reclining patient, **carefully,** in all directions with the flat of the hand. Undue pressure must not be used: it will not accentuate the puckering, and may stimulate metastasis.

Puckering of the skin is seen as a normal finding, particularly in the breasts of multiparae, and also in pendulous breasts, but this puckering is symmetri-

cal and more widespread. Absence of puckering does not negate the possibility of cancer.

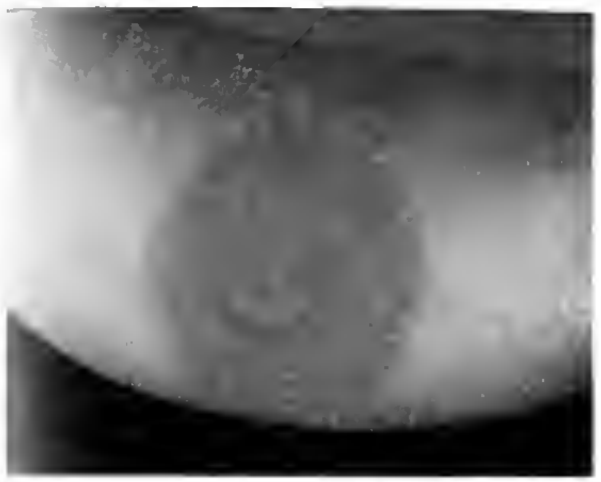
Palpation of the Tumor—In malignant tumors of the same pathologic type, generally speaking it may be said: The smaller the tumor, the better the outlook for complete cure. To be more specific, it is vitally important to discover malignant tumors in the breast before they reach a diameter of 3 centimeters.

Carcinoma of the scirrhous type exhibits a firmness not found in any normal soft tissue. It is usually well delineated, but with irregularities in contour. In certain other types of mammary carcinoma, a deceptive smoothness and roundness may be felt in the tumor delineation.

The palpable lump may be preceded by a stage in which apparently isolated nodules are palpable. This sign may also be produced by benign tumors. When due to cancer, it is an early one.

FIGURE II

Paget's Disease



Eczematous changes confined to the nipple should arouse suspicion of Paget's disease
(Courtesy of What's New, March, 1946)

A single lump should always lead to a suspicion of cancer. Multiple lumps or nodularities, in one or both breasts, reduce the likelihood of cancer, but do not eliminate the possibility.

Malignant tumors usually are not freely movable in the breast tissue, as benign tumors are. Even when the contours of a malignant neoplasm can be readily delineated, the tumor cannot be displaced without concurrent displacement of the breast tissue. Nor does the skin slide freely over a malignant tumor, as it does over a benign one. Rather, it clings to and moves with the underlying tumor and intervening tissues.

If the tumor and the pectoralis major muscle are fused, abduction of the outstretched arm of the affected side to the horizontal position, while holding an object weighing several pounds in the hand, will force the breast outward and upward.

Lymph Nodes—Hypertrophied, hard, discrete lymph nodes in the axilla, lateral thoracic wall or the supraclavicular fossa, sometimes tender on palpation, must be looked upon with great suspicion, but a word of caution is necessary here. **All hypertrophied and hard lymph nodes are not cancerous; cancerous nodes may not be enlarged; and the nodes themselves may show neither macroscopic nor microscopic malignant changes, yet the lymphatic vessels may be engorged with cancer cells.** In summary: hard, palpable lymph nodes are to be regarded with suspicion, but their absence must not alleviate suspicion aroused by other findings.

The Diagnosis

If the attending physician has found a breast tumor which might be cancerous, he should begin cooperation with a pathologist at once. Biopsy is so essential that it should be performed at once, with everything ready for immediate radical resection, if the report confirms malignancy in the tumor. If the biopsy proves negative, the patient should remain under close observation until it is safe to cast off all suspicion.

THE FEMALE GENITAL TRACT

Most cancers of the female genital tract (about 90%) originate in the uterus—corpus and cervix. The cervix is the primary site much more often than the corpus. This might appear, at first glance, to be contradictory to the statistics in Table I of Bulletin No. 2, but that table refers only to **cancer mortality** while the foregoing statement refers to total incidence. From this it must be concluded that many more cervical cancers are diagnosed early—and cured—than is the case with cancer of the uterine corpus.

That, no doubt, is to be expected. The cervix is visible as well as palpable, so that minute, early changes are readily discoverable. On the other hand, the body of the uterus is palpable by bimanual examination, and neoplastic changes should be recognized early, provided the patient herself does not delay the examination.

Refer once more to Chart V, Bulletin No. 1, The Challenge. That chart indicates that 75 to 80% of all cancers originating in the corpus and cervix uteri are curable if discovered early and given adequate treatment without delay—a conservative estimate. **Few organs furnish so excellent an opportunity for early diagnosis as the female genital organs** because (1) they are easily accessible to inspection, palpation, and biopsy, and (2) premonitory symptoms appear early—it is only necessary that patient and physician take the warning seriously. A fortunate feature of cancer of the corpus uteri is its tendency to remain long localized, either in the uterus itself or adjacent tissues.

The Vulva

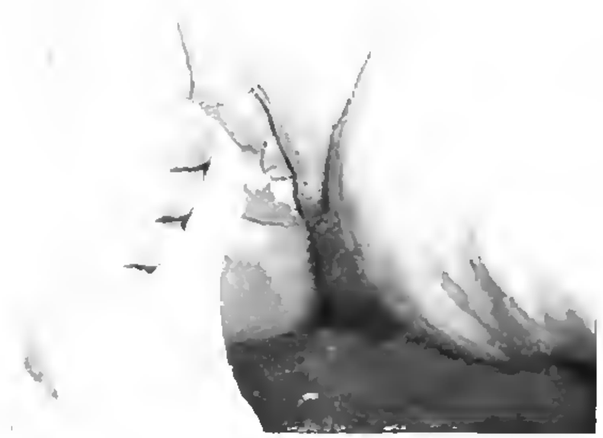
It has been stated that tumors of the labia "are so evident that they cannot be missed." Experience, however, has shown that this apparent truism does not hold. Vulvar tumors are among the most neglected of tumors. Cancer of the vulva is not commonly diagnosed early—and it is by no means rare—but fortunately it is slow-growing and not highly malignant. So little discomfort is experienced in the early stage that a year, or even two years, may pass before the patient pays any real attention to it.

Vulvar pruritus of long duration, **leukoplakia** on the skin of the vulva, or a small area of **thickened epidermis,** with itching—in a woman in her cancer-susceptible years—should arouse suspicion. If cracks or fissures appear and develop into a resistant indolent ulcer, biopsy is definitely in order.

Papules, vesicles, or **warts,** single or multiple, usually **on or between the labia,** may be the first evidences of cancer. Hence, the labia, prepuce and clitoris must be well cleansed and exposed for careful inspection, in order not to overlook any early manifestation of cancer.

FIGURE III

Cancer of the Right Labium



Courtesy of [illegible], M.D., [illegible] Tumor Clinic, Michael Reese Hospital, Chicago

No less important is the **examination of the urethral orifice.** Slight pressure may reveal a node and produce a slight amount of blood-stained discharge from the ulcerated surface of a neoplasm. The **Bartholinian glands** should also be palpated; they are sometimes primarily invaded.

Pruritus is so frequently a premonitory symptom of cancer that every woman in her cancer-susceptible years should be questioned closely, when a history is taken, in regard to any periods of vulvar itching she may have experienced. If there is a positive history of pruritus, do not slight the suggestion. Examine the vulva carefully.

The Vagina

Vaginal cancer may be primary or a metastatic extension from cancer in an adjacent organ. When metastatic, it represents a late stage of the primary growth, even though the vaginal neoplasm is the first indication of cancer encountered. Hence, it is important to differentiate between primary and metastatic cancer when cancer of the vagina is discovered.

Bleeding and leukorrhea are two of the prominent earlier symptoms of vaginal cancer. Inasmuch as the etiologic factor behind leukorrhea may be located anywhere from the vulva to the fallopian tubes, the significance of **leukorrhea** as a symptom of cancer **in any of the segments** of the genital tract will be dealt with here.

Leukorrhea—Leukorrhea may be the initial symptom in cancer of the vagina, cervix, or body of the uterus; it may be the only manifestation for several months. Bleeding is not necessarily an early symptom; it may not even be a cancer symptom, at all. Neither is it necessary that the leukorrheal discharge be bloody, or even blood-tinged, to be a sign of cancer.

Leukorrhea in a woman in her forties, who previously had no significant discharge, should not be lightly dismissed, even though there is no evidence of bleeding. Rather, it should arouse suspicion, and a most thorough examination of the genital tract should be made before instituting treatment, in order to insure against overlooking a possible cancerous origin.

Foul-smelling vaginal discharge is a late symptom. The leukorrhea encountered as an early manifestation of cancer is of typically normal appearance.

The Cervix and the Corpus Uteri

The significance of bleeding as an early sign of uterine cancer cannot be overemphasized.

Abnormal bleeding, **before the menopause,** is indicative of cancer in only a small percentage of cases. Menorrhagia is frequently caused by simple myoma, but **intermenstrual bleeding may be due to malignant neoplastic growth.** Hence, it must be considered and ruled out before instituting therapy.

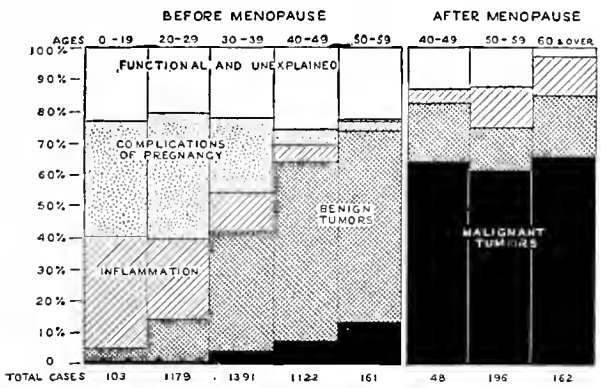
Irregular bleeding, during and after the menopause, indicates cancer more often than not. In the transitional period, occasional bleeding may represent either isolated recurrences of normal menstruation or pathologic postmenstrual hemorrhage. Do not be satisfied to call it the former until a thorough examination assures you of the absence of cancer or some other pathologic process. Cancer is much more likely than a myoma at this stage.

Chart I demonstrates the relative frequency of various causes of gynecologic bleeding in a series of more than 4,000 cases.

CHART I

Causes of Gynecologic Bleeding

Relative Frequency in 4,362 Cases



Before the menopouse, the percentage of cancer cases is small, but not the actual incidence. This will be opparent if you scan the figures, indicating total number of coses, for each column.

(Courtesy of Dr. H. C. Taylor, Jr., and Dr. R. Millen. From Am.J.Obst. & Gynec. 36:22 (July) 1938.)

Before the menopause, malignant tumors cause bleeding in only a small but progressively increasing percentage of cases. After the menopause, cancer becomes the main offender; it exceeds in frequency the combined percentages of all other etiologies.

The Cervix

The diagnosis of cervical cancer is not difficult to make. Theoretically, early diagnosis should be the rule rather than the exception, because the cervix is readily visible through a speculum, and biopsy is easily done in the early stage, without requiring hospitalization.

Practically, however, early diagnosis is not the rule. The chief early symptoms—irregular or postcoital bleeding and leukorrheal discharge—are so lightly regarded by the average woman that she does not consult a physician during the period when early diagnosis and complete cure are possible. Here is an opportunity—and a need—for an educational campaign to impress women with the benefits to be derived from periodic gynecologic examinations, even in the absence of pathologic symptoms, and with the vital importance of reporting any irregularity or unusual occurrence in the functioning of the genital tract.

In about one-third of all cervical cancer patients abnormal bleeding is a late symptom, not early, and there is no leukorrheal discharge. Inspection of the cervix may reveal a small eroded spot, perhaps a result of local irritation from an unhealed childbirth laceration, or a cervicitis.

Only biopsy is capable of revealing the malignant character of such seemingly insignificant lesions. Therefore, do not waste time by a trial of local treatment, and resorting to biopsy only after treatment proves futile. Do the biopsy first; it is a simple and harmless procedure, while the possibility of error resulting from dependence upon inspection alone may carry with it a fatal risk.

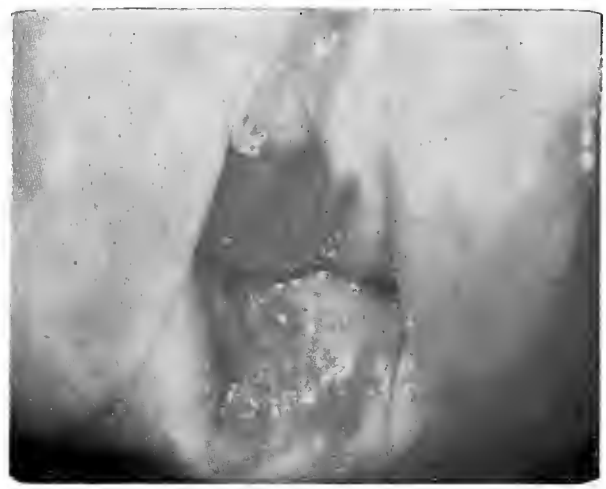
Cervical biopsy can be done with a simple biopsy punch. Special equipment is not, however, essential. A small sliver of tissue can be removed with a scalpel. This causes little or no pain because the cervix is relatively insensitive to pain. Bleeding is usually minimal; it stops spontaneously or after a few moments of pressure with gauze against the bleeding point.

The removed tissue should be placed immediately in a 10% solution of formalin (obtainable at any drugstore), and sent to a reliable laboratory for microscopic examination and diagnosis without undue delay.

The Schiller Test—The Schiller Test utilizes the fact that normal cervical and vaginal epithelial cells of the sexually mature female store glycogen. By painting or rinsing the cervix and surrounding mucosa with Gram's iodine solution (iodine, 1 part; potassium iodide, 2 parts; water, 300 parts) or with ¼ strength tincture of iodine, normal squamous epithelium takes on a deep brown discoloration, making nonstaining areas (erosion, cervicitis, cancer, etc.) more conspicuous than before by contrast.

FIGURE IV

Cancer of the Cervix Uteri



The malignancy of this benign appearing lesion was revealed only by biopsy. (Courtesy of *What's New*, March, 1946)

The test is not applicable before puberty and is of little value about three years after the menopause, because of the absence of glycogen in these periods.

The value of the Schiller test consists primarily in calling attention to a suspicious spot which might

otherwise have been overlooked. A positive test does not establish a diagnosis of malignancy, nor does a negative test rule it out. Biopsy alone is conclusive.

Cytologic tests of cervical and vaginal smears promise to become an important supplementary method for diagnosis of cancer in the genital tract, and may become a routine office test for early diagnosis.

Urinary symptoms, such as painful and burning micturition, nocturia, increased frequency, or even moderate incontinence may well indicate cancer of the cervix at a curable stage. Although in most women such symptoms might arise from benign causes, they should always prompt exploration of the genital tract for a *possible* malignant origin.

Corpus Uteri

Carcinoma of the corpus uteri originates in the endometrium. It tends to produce intermenstrual and postmenstrual bleeding which may vary from occasional, barely perceptible spotting to profuse flow simulating menstruation.

In spite of the endometrial location of uterine cancer, there may be absence of metrorrhagia and menorrhagia; in the initial stages, bleeding may occur only in response to provocation, such as pelvic examination. Hence, absence of bleeding does not prove that there is no cancer present, while the slightest bleeding—even if observed but once—should create suspicion, and calls for thorough investigation of the genital tract.

Postmenopausal bleeding, unless caused by cervical polyps, is almost pathognomonic of cancer. The significance of leukorrhea has been discussed.

Inasmuch as biopsy provides the only certain method for diagnosis, curettage should be done without delay in older patients when there is anything to cause the least suspicion. In younger patients with uterine bleeding, diagnostic curettage is indicated when the bleeding has failed to react favorably to therapeutic measures in a short time.

Cancer of the uterus occurs with increasing frequency after cessation of ovarian function. Myoma uteri occurs most often in the period of sexual maturity. In a small number of women, myoma and cancer occur concomitantly. Rarely, malignant degeneration of a myoma takes place. Hence, during the menopause the presence of a myoma accompanied by irregular bleeding should not be accepted as evidence of absence of cancer, and an increase in size of the myoma at that period should be viewed with suspicion. Utilize every possible method; particularly have a pathologist examine curettage material to eliminate cancer before accepting myoma as the cause of the bleeding.

Early carcinoma involves only a small area. Hence, the diagnostic curettage must be *thorough*, albeit gentle, after good cervical dilatation. In contrast to cervical biopsy, curettage is not an office procedure. It must be done in a hospital, under anesthesia, but requires only a short hospital stay.

If no cancer is found after competent curettage, both the patient and the physician may feel secure. Furthermore, the operation may prove helpful in a positive way, because curettage is often of curative value in premenopausal functional bleeding, the condition most frequently requiring differentiation from intra-uterine cancer.

Lymph Nodes—The only genital tract nodes accessible to inspection and palpation are the inguinals, into which are drained the lymphatic channels from the fundus uteri, the lowest part of the vagina, and the labia.

FIGURE V

Cervical Lesion—Benign or Malignant?

Cancerous appearing ectropion, eversion and erosion, proved benign by biopsy. (Courtesy of *What's New*, March, 1946)

Parametrial Palpation—Impairment of uterine motility may be due to simple inflammatory changes in the parametrium. On the other hand, cancer may invade the parametrium without causing induration. In other words, no reliance is to be placed on palpation as a guide for determining the spread of uterine cancer into the parametrium and broad ligaments. It is futile and dangerous to attempt to define the stage, extension, or prognosis of cancer from evidence furnished by palpation.

The next issue of the BULLETIN will discuss "The Early Diagnosis of Cancer of the Tongue, Parotid Gland, Larynx, Thyroid, and the Bronchopulmonary Tract."

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. 1 NO. 5

EARLY DIAGNOSIS OF CANCER OF THE TONGUE, PAROTIDS, LARYNX, THYROID, and BRONCHOPULMONARY TRACT

In this issue it has been deemed fitting to consider cancer of the bronchopulmonary system in connection with cancers affecting certain organs adjacent or related to this tract.

THE TONGUE

It would seem that the location, function, and sensory characteristics of the tongue would make early recognition of cancer in that organ almost certain in most instances. The organ itself is easily accessible for inspection and palpation; it is highly sensitive to pain and the slightest discomfort; it is endowed with the sense of touch; it has a highly diversified motile activity which produces many variable forms and exposes it to pressure from many directions. Nevertheless, there is a lapse of six months, in the average patient, between the first manifestation of lingual cancer and the appearance of the patient in a hospital for treatment.

Leukoplakia may be a warning sign. It is not cancerous itself but may be a precursor.

The **early cancerous tumor** of the tongue is either a firm, wartlike, papillary lesion or a small, slightly elevated lump. They may be multiple from the start. When fully developed, the infiltration extends well beyond the palpable and visible range.

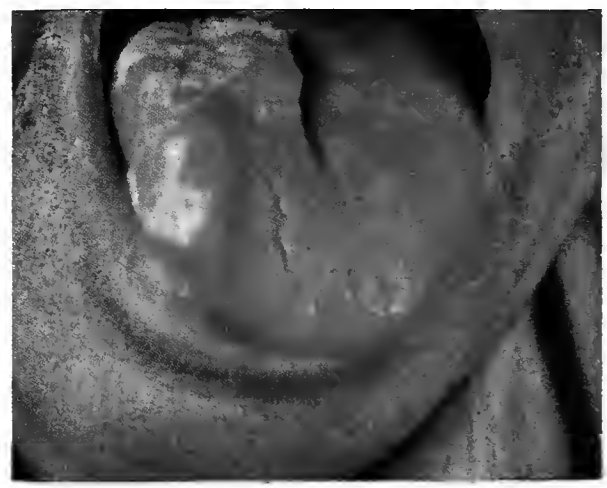
If the neoplasm becomes ulcerated, **pain** is an early symptom. The pain is usually of the intermittent type, increasing when the ulcer is irritated, chemically or mechanically, by food or drink. However, it may be an intense, constant, and gradually increasing pain, referred to an ear, uninfluenced by local irritation of the ulceration. This pain may suggest otitis media. Hence, when such pain is encountered and no cause is found for it in the auditory apparatus, the tongue should be inspected and palpated.

Slight **lateral deviation of the tongue,** without neurologic cause, is another early symptom that may be encountered.

Fetor, hemorrhage, salivation, and **edema** are **later symptoms** in cancer of the anterior portion of the tongue.

Cancer of the **posterior portion** of the tongue may exist for a long time before it produces alarming symptoms. There may be nothing more than a history of repeated attacks of **"sore throat."** The attacks, however, become more frequent and more prolonged, until at last there are no intervals of freedom. This type of cancer is generally accompanied by **salivation** with a backward flow which evokes a persistent desire to clear the throat.

FIGURE 1
Leukoplakia of Tongue



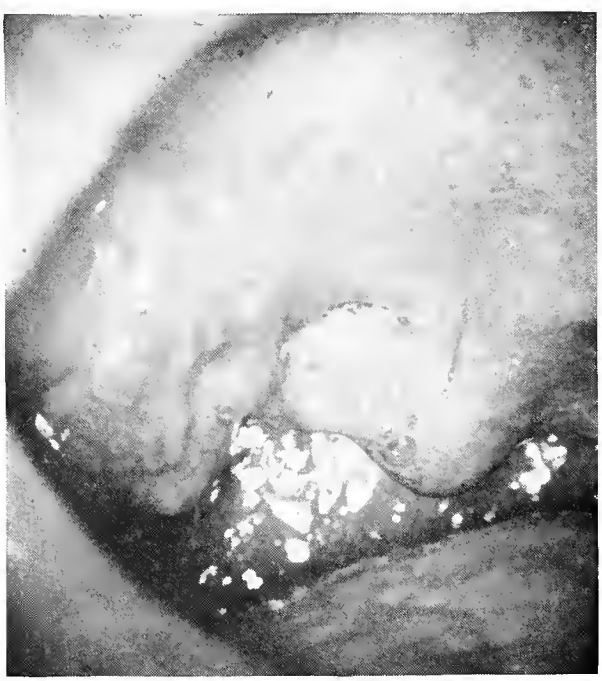
(Courtesy of *What's New*, March, 1946)

Occasionally, the **sputum** is spotted or streaked with blood, and there may be slight dysphagia.

Dysphagia is always an alarming symptom to the alert physician, but not always to the patient. The patient may get accustomed to it and not even report it. Hence, inquiry about difficulty in swallowing should always be made in suspected cases.

When the regional lymph nodes are involved by metastases, the chances of cure are greatly reduced, but not necessarily excluded. Metastases may occur early or late. Lymph nodes may be invaded without showing enlargement, whereas firm, hypertrophied glands are not necessarily already invaded. Biopsy alone can establish the fact of invasion. The most important groups of lymph nodes to be checked, in

FIGURE II
Early Cancer of Soft Palate



(Courtesy of P. H. Holinger, M. D., St. Luke's Hospital, Chicago)

lingual cancer, are the submaxillary, submental, and cervical (superficial as well as deep).

THE PAROTID GLAND

Malignant tumors of the parotid gland are rare, but are so readily recognizable in an early stage, when occurring, that there is little excuse ever for allowing such a tumor to reach an incurable stage. **Virtually every death from cancer of the parotid gland is preventable.**

Whenever a small lump is noted in the parotid gland of a patient, probably incidental to a general examination, an investigation should be made. The lump may cause neither pain nor discomfort, but that does not alter its significance.

Such a small tumor may persist for years, with no apparent change, when suddenly the patient becomes aware of slight discomfort, a tension when chewing, and some enlargement. At this stage, it is still not too late—complete surgical removal will effect a cure. If this is not done promptly, and the encapsulated stage is allowed to pass, the patient is doomed, because the mixed salivary gland type of cancer is one of the most malignant of all cancers.

Parotid tumors, when first seen and palpated, are (1) elastically solid, (2) hard, or (3) soft in consistency. An elastic tumor may be a cyst with a salivary calculus which will show on an x-ray film. A hard tumor is more than likely a mixed salivary tumor, potentially malignant. **The softer the tumor, the greater the malignancy:** the softness is indicative of a preponderance of embryonic tissue.

THE LARYNX

The incidence of laryngeal cancer is increasing. Why, we do not know. Sex preference is definite—about 90% occur in males. No age is immune, but the peak of recognized cancers of the larynx is found in the ages from 50 to 60 years.

The chances of cure are about 80% when the diagnosis is made early, but late diagnosis virtually always ends fatally.

Symptoms—The larynx is concerned with two bodily functions—respiratory and phonetic. The latter is impaired in the early stage of the disease in 95% of cases, as indicated by **hoarseness.** The initial hoarseness, like the initial sore throat in cancer of the tongue, is slight and intermittent, but gradually becomes more intense and more persistent. In modern living there are many causes for hoarseness, such as excessive smoking, chronic sinusitis, and straining of the voice in noisy environments. In spite of many possible explanations, any patient complaining of persistent and increasing hoarseness should have the benefit of a special examination and investigation immediately, with the thought of a possibly malignant etiology in mind. Further, whenever a patient complains of ear, nose, or throat trouble, the larynx should be routinely examined.

Even before the appearance of hoarseness, such **seemingly trivial symptoms** as undefinable discomfort or "tickle" in the throat and the sensation of a small lump in the throat experienced on swallowing (a pre-stage of dysphagia) should call for an examination of the larynx.

Pain, dyspnea, fetor, excessive salivation and blood-streaked secretions from the throat are late symptoms which, almost invariably, have been preceded by some of the early signs. This is particularly true in intrinsic laryngeal cancer which originates in the true vocal cords. In extrinsic laryngeal can-

cer, originating on the posterior surface of the epiglottis, pain may be an early symptom because the lesion is more exposed to pressure on the swallowing of solids.

Of the various diagnostic procedures applicable in connection with laryngeal examination, five are within the scope of the general practitioner:

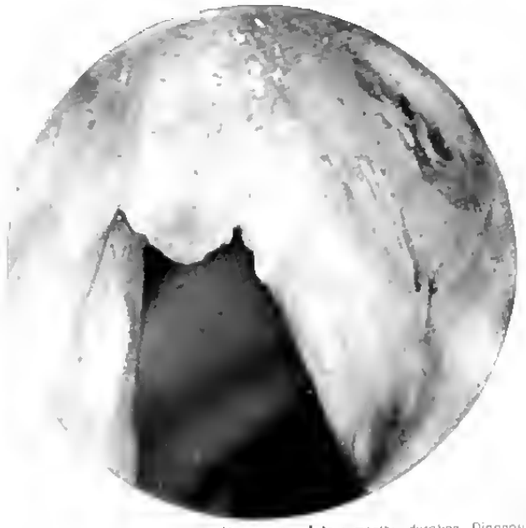
1. History
2. Palpation of neck and external laryngeal region
3. Mirror examination of the larynx
4. Blood examination (Wassermann, Kahn)
5. Chest x-ray

In taking the history, the patient should be questioned particularly in regard to the symptoms previously discussed: hoarseness, discomfort in the laryngeal region, "tickle" in the throat, dysphagia, sensation of a lump in the throat, pain, dyspnea, fetor, excessive salivation, and blood-streaked secretion.

External palpation in the laryngeal region should determine asymmetries or unilateral thickening—both are early signs—or tenderness which indicates perichondritis, a late symptom.

A well-marked lesion is readily detectable through **mirror examination** of the larynx, but a negative

FIGURE III
Laryngoscopic Diagnosis



Cancer of Anterior Commissure—Hoarseness of four months' duration. Diagnosis could have been made much earlier by laryngoscopic examination. Even so, laryngectomy resulted in cure.
(Courtesy of P. H. Bolinger, M. D., St. Luke's Hospital, Chicago)

mirror examination does not necessarily rule out cancer. The anterior commissure and the posterior surface of the epiglottis are not always clearly enough visualized to permit the finding of minute lesions, and the malignant lesion may escape attention through "mimicry," exhibiting the pink of the laryngeal mucosa on the whitishness of the vocal cords. Hence, it should be made a rule to refer to a specialist any patient who presents even a remote possibility of having laryngeal cancer. The specialist

FIGURE IV
Laryngoscopic Diagnosis

Early Cancer of Anterior Two-Thirds of the Right Vocal Cord—Hoarseness of 6 months' duration. Diagnosis could have been made several months earlier. Surgical removal of right vocal cord resulted in cure.
(Courtesy of P. H. Bolinger, M. D., St. Luke's Hospital, Chicago)

has other and more highly specialized means of examination at his disposal.

It may be necessary to reassure a patient, who has more fear of losing his voice than his life, that **it is possible to speak satisfactorily without a larynx**, and that the new voice will sound quite natural except for some degree of hoarseness.

THE THYROID

Like laryngeal cancer, the incidence of cancer of the thyroid is on the increase. It is quite possible that this is more apparent than real, however, because of improved diagnostic measures and the increased frequency of surgical treatment of this gland.

The thyroid suffers pathological changes in women much more often than in men. Hence, it is not surprising to find that thyroid cancer incidence is also much higher in women. There is one noteworthy feature regarding its age distribution: **the high incidence in the younger years of life.** Approximately 10% occur in patients under 30 years of age, and more than 50% in patients under 50. In other words, about one-half of the cases of thyroid cancer occur before what are generally regarded as the cancer-susceptible years.

Thyroid cancers most often result from malignant

degeneration of erstwhile benign thyroid adenomas. This would suggest that **routine surgical removal of adenomas** of the thyroid should be practiced as a prophylactic measure, because about 5% of adenomas show beginning malignant changes when microscopically examined. They may remain benign for several decades before they show sudden increase in growth and hardness which suggest malignant degeneration.

When this sudden hypertrophy occurs, cancer must be differentiated from massive hemorrhage into the adenoma—a frequent occurrence. Differential diagnosis rests largely on two features:

1. The development of hemorrhagic enlargement is much more rapid.
2. The tumor has a stony hardness in cancer, whereas there is some elasticity to the hardness of a hemorrhagic tumor.

Suggestive signs of carcinoma are compression of the trachea and an indefinite, mild dysphagia which are not compatible with the small size of the visible and palpable tumor.

Thyroiditis is so rare that it plays an insignificant part in differential diagnosis. The real difficulty, the circumstance which is most likely to cause delay in diagnosis, is the fact that cancer most often develops in a gland which previously has been known to be abnormal. Adenomas occur frequently in colloid goiter, and the enlarged gland is firm and sometimes asymmetrical. Some adenomas are poorly encapsulated; in some, fusion occurs between discrete tumors, some become necrotic and form cysts; altogether, adenomas present a number of diagnostic problems. Therefore, it is often difficult to evaluate such criteria as hardness, roundness, tenderness, and even free motility of the tumor.

Fusion of the tumor mass with the skin is virtually pathognomonic of cancer, however.

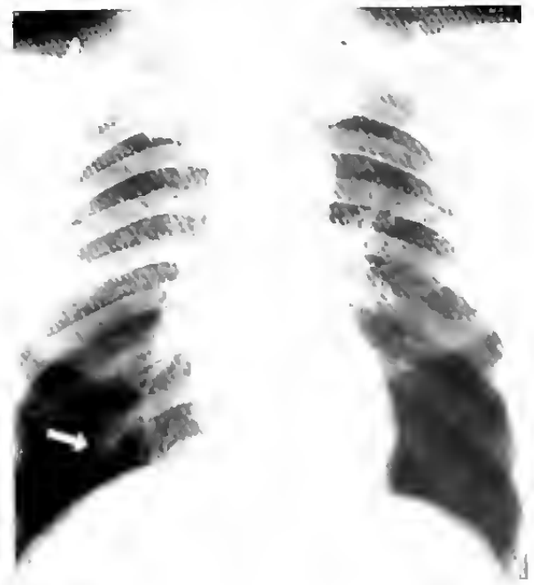
Because of the diagnostic difficulties, it should be emphasized that practically all cancers of the thyroid are coincidental with thyroid tumors of other types. Thyroid surgery has been developed to such a high degree of perfection that the surgical risk accompanying the removal of these tumors is almost negligible. Hence, **thyroid cancer could probably be reduced to a rarity** if all thyroid tumors were routinely removed when diagnosed.

The general outlook for patients with thyroid cancer, diagnosed when still in the stage of limited infiltration beyond the adenomatous origin, is still excellent under surgical treatment.

THE BRONCHOPULMONARY TRACT

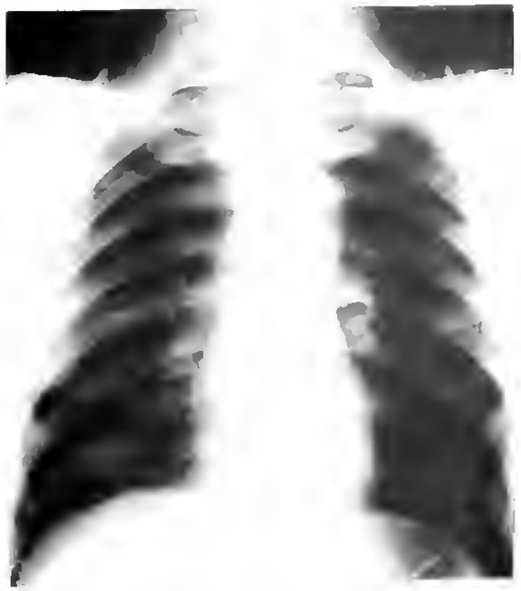
As shown in Table I of BULLETIN 2, cancer of the respiratory system—preponderantly of the lungs—ranks fourth as a cause of cancer deaths in the United States. Incidence is highest between the ages

FIGURE V (a)
Roentgenologic Diagnosis



Early Bronchial Carcinoma—Arrow points to a small patch partly superimposed on shadow of rib. The patch did not arouse suspicion.

FIGURE V (b)
Roentgenologic Diagnosis



Same Patient, several months later. Increase in size of the patch aroused suspicion and tumor was diagnosed.
(Courtesy of Northwestern University Medical School X-Ray Dept.)

of 40 and 60 years, with a definite predilection for males. Whether there is a causal relationship between the higher incidence in the male and the more widespread habit of smoking and inhaling among men is a moot question.

In the vast majority of cases, the tumor originates in a bronchial wall; primary development in the interstitial tissue is exceptional. This preference for the bronchi favors early diagnosis, because the impeded flow of air through the bronchial lumen engenders a series of symptoms which depends upon the site of the tumor, the size of the bronchus involved, and the progress in bronchial obstruction.

Pathogenesis

At first there may be a **slight wheezing** which persists even after considerable expectoration, so long as obstruction is incomplete.

Sometimes, through a ball-valve-like effect, a peculiarly **localized emphysema** may result; this may be masked in the aged, however, by a general emphysema already present.

When obstruction is complete, **localized atelectatic collapse of lung** tissue may occur, or bronchiectatic changes may predominate. Infection of these areas frequently follows.

In general, the development of pulmonary cancer has the characteristics of a slowly developing and expanding infiltrative process, lacking in any specific symptom except, perhaps, continuous cough. Necrotic changes in the tumor may result in abscess formation.

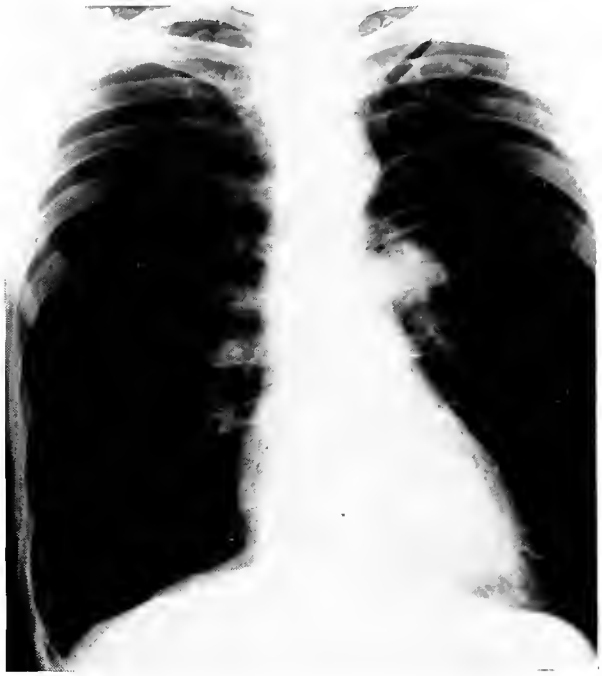
Symptomatology and Diagnosis

Cough is the most constant and persistent symptom. It is chronic and more or less continuous, or it may occur in paroxysms, simulating pertussis. Expectoration may be mucous or purulent, even blood-streaked if the mucous membrane of the bronchial wall is ulcerated.

Any patient with a persistent, chronic cough, or with evidences of prolonged, nonresolving pneumonia, or even with persistent and resistant simple bronchitis should be thoroughly investigated for possible pulmonary cancer. The diagnostic difficulties may be complicated by signs of pulmonary abscess, due to necrotic changes in the tumor, and blood-streaked sputum or even full-fledged hemoptysis suggesting a tuberculous infection. Indeed, tuberculosis may coexist with the cancer, and mask the malignant disease.

Pain is not a constant symptom. It is most often due to pleural irritation from a tumor with a peripheral site or one which has spread to the periphery. The type and location of the pain depend upon the part of the pleura involved.

FIGURE VI (a)
Roentgenologic Diagnosis



Early Bronchial Cancer—Left Hilum, Anteroposterior View.

FIGURE VI (b)
Roentgenologic Diagnosis

Some Patient, Lateral View—Pneumonectomy resulted in cure.
(Courtesy of Paul H. Holinger, M. D., and Willard Van Hazel, M. D., St. Luke's Hospital, Chicago)

If a tumor in the basilar portion of the lung irritates the diaphragmatic pleura, the pain will be felt in the area controlled by the distribution of the phrenic nerve. In some instances, eating will evoke pain only at the particular moment that the peristaltic wave of the esophagus passes the diaphragmatic hiatus.

When the tumor is located in the apex of a lung, the initial stage of Horner's syndrome may be the first indication, or the patient may report to his physician because of **"rheumatic" pain in the arm.** Another area of pain is located between the scapulae; a history of such pain may be reported by the patient, or the pain may be evoked by the examiner by scratching on either side of the thoracic vertebral column.

When pain is due to pleural irritation it disappears if an exudate appears and separates the pulmonary from the parietal pleura.

The character of pleural exudation is not specific in cancer. A sanguineous exudate may or may not be caused by cancer, but it should certainly arouse suspicion. A serous exudate, on the other hand, should not allay suspicion, because it, too, could be caused by cancer.

X-ray examination of the chest is essential in every case of suspected pulmonary tumor. The radiologist, unfortunately, is confronted by some of the same difficulties as the clinician. There are no specific radiologic signs of tumor. Hence, it is of prime importance that the clinician and radiologist co-operate closely. The radiologist should be informed of the exact location of abnormal breath sounds, or areas of dullness or other abnormality found on physical examination. **A routine chest film is not sufficient;** it may be negative, whereas fluoroscopy with the patient in various positions may reveal a suspicious shadow which should then be confirmed by a roentgenographic film taken with the patient in the same position.

Next in importance is **bronchoscopy.** More than three-fourths of all pulmonary cancers are recognizable by the bronchoscopist—and in their earliest stage—by **bronchoscopic biopsy.** The method should be used more frequently. In the hands of a competent specialist the risk involved and the discomfort suffered by the patient are certainly no greater than in cystoscopy.

In summary, it may be said that routine use of the x-ray and the great progress made in bronchoscopic technic have contributed more than anything else to early diagnosis in cancer of the lungs. Even so, early diagnosis is still more dependent upon alertness on the part of the examining physician than any diagnostic facility available. Unless his suspicion is aroused by seemingly insignificant symptoms, even the best diagnostic methods will fail, and the cancer mortality will not be reduced.

Treatment

The mortality rate in pulmonary cancer is extremely high. Life-saving therapy is restricted to the few in whom early diagnosis is established. Radiotherapy appears to be ineffectual.

Pulmonectomy appears to be the only effective remedy. Formidable as this operation is, its technic has become so perfected that, in the hands of an expert, its benefit should not be denied even to aged patients with pulmonary cancer. Patients even in the seventh decade of life have been cured by such radical surgery. This makes early diagnosis worth striving for.

●

FOR YOUR INFORMATION

Although diet has no bearing on early diagnosis of cancer, the possibility of a relationship existing between cancer and diet (quantitative as well as qualitative) is of enough fundamental interest to warrant a few words of discussion. Recent work in this field of cancer research is full of promise.

The quantitative aspect is supported by an analysis of life insurance statistics which suggest that increase in cancer mortality accompanies increase in body weight. Findings in experimental cancer point in the same direction. Growth rate, as well as incidence, of tumors, whether spontaneous or induced, can be reduced when caloric intake is restricted. A greater caloric restriction is required to delay development of an established new-growth than to reduce tumor incidence.

In support of the qualitative aspect, it has been shown that a high fat diet exerts a specific stimulating influence on the incidence of spontaneous breast tumors in animals. Certain vitamin deficiencies also influence tumor incidence one way or another. Riboflavin deficiency increases the incidence of induced hepatomas in rats, while biotin or pyridoxine deficiencies exert an opposite influence.

Another interesting observation calls attention to the possible relationship between dietetic irritation, gastritis, and gastric cancer. While the *total* cancer incidence in England is the same as in Holland, the incidence of gastric cancer in Holland is approximately twice as great as in England. Certain differences in the dietetic habits of the nations may be significant in this regard. The Dutch people consume more roughage, spices, spirits, and tobacco, and tend to eat their meals hotter. They also show a higher incidence of oral sepsis.

●

BULLETIN No. 6 will present an article on "Early Diagnosis of Cancer of the Urogenital Tract."

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 6

EARLY DIAGNOSIS OF CANCER OF THE UROGENITAL TRACT

The title of this article is a bit more inclusive than it should be, because cancer of the uterus and lower female genital tract was dealt with in BULLETIN No. 4, and will not be repeated here. The ovary, the male genital organs, the kidney, and the bladder will comprise the subject of this discussion.

THE OVARY

Strictly speaking, early diagnosis of ovarian cancer is possible only as an incidental finding during surgical exploration of the pelvis. Cancer of the ovary is symptomless in its early stage; physical examination is not revealing. And yet, **the ovary is probably the most fertile organ in the body when it comes to producing new-growths** of many and various types, a relatively high percentage of which are or become cancerous. Metastatic cancer in the ovary is also a frequent occurrence.

Symptomatology and Diagnosis

Inasmuch as early diagnosis of ovarian cancer is usually a postoperative finding (pronounced by the pathologist), the clinical symptomatology and diagnosis could best be discussed in terms of any ovarian tumor. Since this might not be altogether satisfactory, the general discussion of clinical signs and symptoms will be supplemented by a short discussion of the more important ovarian new-growths, grouped according to histogenesis.

Backache is so common in women that many of them disregard it. Yet, it may result from the weight of a neoplasm. The ache may be unilateral or bilateral, depending upon the position of the tumor.

Pain should always be given serious consideration. It may be dull when due to tension or adhesions; it may simulate ureteral pain when a pediculated tumor tugs at its pedicle; or it may be intensely acute if a cyst ruptures or a pedicle is twisted.

Vesical symptoms may occur but not commonly.

Menstrual symptoms are not common. When present, they follow no rule, and bear no relation to the size of the tumor.

Gastrointestinal symptoms, such as anorexia, nausea and vomiting, indigestion, belching, flatulence, and constipation, are equally inconstant. These complaints are so frequent and indefinite that they may be disregarded by both physician and patient. They are useful for tumor diagnosis only when gynecologic examination is made a routine procedure in instances of otherwise unexplained gastrointestinal symptoms.

Cachexia, loss of weight, and hypochromic anemia usually indicate cancer, but some benign ovarian tumors, particularly when associated with ascites, may cause cachexia. Hence a tumor of the ovary associated with cachexia cannot be automatically assumed to be a malignant tumor in a hopelessly advanced state.

A palpable pelvic or abdominal mass, palpable enlargement of an ovary, visible increase in the size of the abdomen due to the size of the neoplasm or to ascites which frequently accompanies ovarian tumors—these are still the most reliable signs, but late ones, of ovarian tumor.

Special Tumors

Serous Cystadenoma (Including Semi-solid and Solid Variants)—Although the great majority of tumors of this group are benign, clinically as well as pathologically, no absolute reliance can be placed on this prevalent behavior. In some types widespread peritoneal dissemination occurs, associated with ascites, indicative of a low order of malignancy.

Tumors of this group, with an age incidence of twenty to fifty years, make up approximately one-sixth of all ovarian new-growths. They do not occur before puberty. They are more often unilateral than bilateral and, when solid, may be mistaken for ovarian fibromas.

Pseudomucinous Cystadenoma—Clinically, these tumors comprise approximately twenty to thirty

per cent of ovarian neoplasms. Like serous cystadenomas, they are extremely rare before puberty, and uncommon after the menopause.

It is amazing to note how much apparent destruction of ovarian tissue this tumor can cause without disturbing the menstrual function and without interfering with fertility. It is generally unilateral, and sometimes gives rise to ascites or hydrothorax. Some forms of this tumor appear to be malignant.

Primary Carcinoma of the Ovary—In women who have reached the menopause, more than half of all ovarian new-growths are cancerous.

Unfortunately, there are no symptoms in the incipient stage of carcinoma of the ovary. Pain—which may result from peritoneal irritation, direct mechanical pressure, nerve invasion, torsion of the ovary, or ileus—is, in many instances, the first, yet a late, symptom. Ascites, hydrothorax and abdominal enlargement from the expanding tumor also indicate an advanced stage. The incidence of menstrual abnormalities is insignificant where the ovarian carcinoma is of the papillary type but, when encountered, should arouse suspicion just as surely as any abnormal vaginal bleeding or postmenopausal spotting.

It may be impossible, in the course of a surgical operation, to designate a neoplasm as either benign or cancerous from gross inspection. Histologic examination is then imperative.

In many instances **peritoneoscopy** is indicated. In conjunction with biopsy, this offers a two-fold advantage: It is a minor risk as compared with laparotomy in the presence of carcinoma of the ovary (five to ten per cent mortality), and a correct diagnosis can be established through the biopsy.

Ovarian Fibroma—One particular sequela of this usually benign tumor makes its discussion here advisable. Ovarian fibromas, after reaching a diameter of 6 cm. or more, may cause ascites, often of an advanced degree. Since there is a tendency on the part of some physicians to regard any abdominal tumor associated with ascites as cancerous and inoperable, it is important to remember that a benign fibroma may be the causative factor, and should be searched for. The condition is amenable to complete cure by surgical extirpation of the tumor.

These tumors do not assert themselves clinically before puberty. The first symptoms are rarely noted until the tumor has become large enough to outgrow the true pelvis.

Granulosa-Cell Tumors—Although determination of the degree of malignancy of these tumors still presents unsettled problems, the fact that they recur clinically and are capable of metastasizing in a significant number of cases justifies their discussion.

The seemingly contradictory clinical manifestations of this type of tumor can be interpreted only on the basis of the modern understanding of the action of sex hormones.

Granulosa-cell tumors elaborate estrogen, producing a high blood concentration of this hormone. Thus, when originating before the onset of puberty, they cause precocious somatic and sexual development as the most remarkable, and early, indication of their presence.

When they appear after the menopause, the excess estrogen leads to uterine bleeding with some degree of rhythmicity, and to general sexual rejuvenation. In contrast to the continuous spotting of uterine carcinoma, the bleeding from granulosa-cell tumors is intermittent and of larger volume.

Most granulosa-cell tumors appear during the years of full sexual activity. At this time, the high estrogen level in the circulating blood tends to cause amenorrhea. If this phenomenon occurs in the premenopausal years, the cessation of menses may easily be mistaken for the beginning of the physiologic menopause.

Rarely, the tumor gives rise to ascites which, in some instances, is hemorrhagic.

Secondary Tumors of the Ovary—To complicate further the diagnosis of primary tumors of the ovary, **the ovaries are a favorite site for cancerous metastases.** They are particularly prone to receive metastases from the organs in the pelvis proper (the uterine fundus, fallopian tubes, and pelvic colon), and from the upper segments of the gastrointestinal tract, the gallbladder, and the pancreas. It is particularly confusing that the symptoms arising from ovarian metastases frequently are more prominent than those from the primary cancer itself.

For this reason it is extremely important to **consider the possibility of a primary cancer elsewhere within the abdomen** whenever bilateral, solid, lobulated tumors of the ovary are encountered.

Concluding Remarks

The only safeguard against the grave consequences of cancer is the surgical removal of all ovarian tumors encountered. Small cystic tumors, up to 5 cm. in diameter, may be excepted from this generalization, but if they are they should be kept under close observation by occasional examination. The difficulties in differential diagnosis of ovarian tumors, when depending exclusively upon palpation, are formidable. Surgical exploration, visual inspection, and pathologic examination and diagnosis are the only certain methods in most instances.

From a practical standpoint, two considerations will prove helpful:

(a) Any ovarian tumor—solid or cystic, unilateral or bilateral—should be looked on with suspicion until proved innocent.

(b) Every solid ovarian tumor should be removed immediately after diagnosis, because

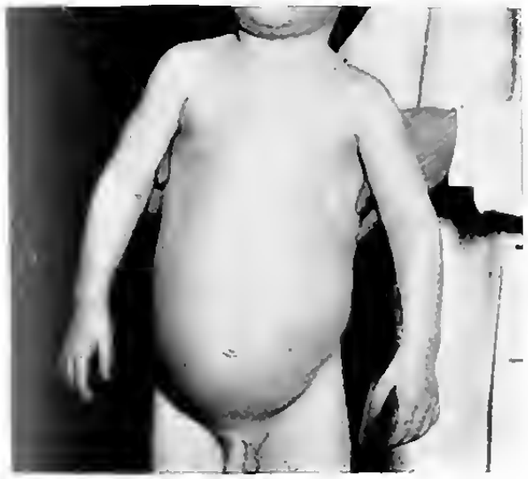
it is in the solid type of ovarian tumor that the most highly malignant cancer is found, and surgical extirpation is the only measure of value.

THE KIDNEYS

For practical purposes it may be considered that there are no really benign renal tumors. There is a **relatively high incidence of renal cancer in children**, a notable exception to the rule. Mortality of renal carcinoma is exceedingly high.

The form usually encountered in children is known as **Wilms' tumor**—embryonal carcinosarcoma of the kidney. It develops most often within the first five years of life. No sex preference is shown.

FIGURE 1 (a)
Wilms' Tumor of Left Kidney



Note the enlargement and irregular contour of the left side of the abdomen.

Early diagnosis of Wilms' tumor—an exceedingly malignant neoplasm—is rare. Few patients have been cured. **The only hope for early diagnosis** lies in suspicion being aroused by (1) elicitation of pain localized over a kidney, or (2) hematuria occurring before invasion of the structures adjacent to the kidney has taken place. Usually, however, the tumor is discovered only after having attained a large size, because of the rapidity of its growth and absence of early symptoms.

In adults, **hypernephroma**—a tumor of the kidney whose structure resembles that of cortical tissue of the adrenal gland—is the usually encountered form of renal cancer. Hypernephroma shows an age preference for the fifth decade, and a decided sex preference for the male.

A leading symptom, whose importance cannot be over-emphasized, is **hematuria.** It is painless, in contrast to hematuria caused by a calculus. The bleeding may be moderate or severe—frequently more profuse than could be expected from a calculus, because of erosion of a blood vessel by the tumor.

Hematuria is usually intermittent and of short

FIGURE 1 (b)
Wilms' Tumor of Left Kidney

Same patient—The protrusion of the abdomen, due to the large tumor, is even more apparent in this view

duration. It may constitute **the only early symptom** and, since years have been known to elapse between the first and second attacks, the life of the patient may hinge on the physician's attention to the **first warning**—the initial attack. The second may occur only after the tumor has reached a stage beyond hope of therapy. Hence, the importance of not waiting for a second attack.

Hematuria, particularly when painless, should lead to immediate investigation of the cause. The more isolated the symptom appears to be, the more intense should the search be. Cystoscopy should be performed before the bleeding has stopped.

Colicky pain may occur during hematuria, secondary to obstruction by blood clots. In about one-third of the patients, there is **a constantly painful sensation,** dull or burning in character, referred to the loin. This is an early symptom and may be the only one during the early stage.

The presence of **a large, palpable mass** usually indicates a late stage, if it is a cancer. It must be remembered, however, that the mass may represent a hydronephrosis **caused by a small cancer,** strategically located, still in its early and curable stage.

Continuous, mild fever of unexplained origin, without a discernible focus or sign of infection, should arouse suspicion of a malignant renal tumor.

In addition to **cystoscopy,** diagnostic procedures of particular value include **intravenous pyelography** and **retrograde pyeloureterography.** These methods do not substitute for each other; they are

supplementary methods, each adding a share of information which cannot be gained by employing any one of them singly.

In the present state of therapeutic possibilities, early diagnosis offers the only means of reducing the high mortality rate in renal cancer.

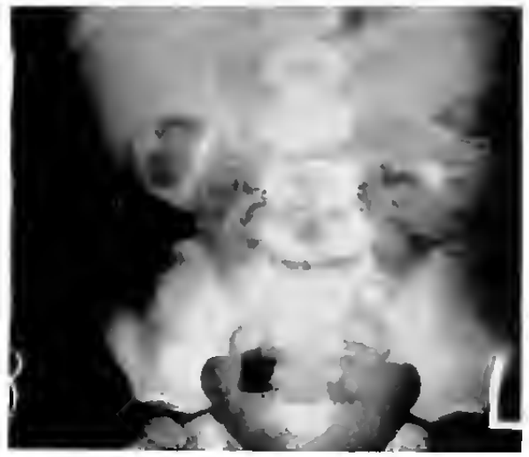
THE BLADDER

Cancer of the bladder offers one diagnostic advantage: It is **usually located at the trigone or at the bladder outlet,** so that even relatively small tumors stir up urinary symptoms. Bladder carcinoma shows a distinct preference for the male sex and usually appears after the age of 50 years.

Hematuria is the most significant and early encountered symptom. In a considerable number of patients, hematuria indicates cancer in some part of the urinary tract; about one-half of the time, microscopic bleeding is due to a bladder tumor. The points previously brought out about hematuria apply here as well.

Frequency of micturition and painful urination are later symptoms than hematuria. If engendered

FIGURE 1 (c)
Wilms' Tumor—*Roentgenologic Diagnosis*



Same patient—Intravenous pyelography corroborates the presence of a kidney tumor on the left side

by infection (which invariably follows obstruction at the bladder outlet) they are definitely late symptoms.

If ureteral occlusion occurs, symptoms of hydronephrosis (usually infected) predominate. Bilateral obstruction leads to renal insufficiency and eventuates in uremia.

Cancer of the bladder and prostatic hypertrophy have the same age incidence and several common clinical manifestations, and are not infrequently concomitant. This association may cause the cancer to be overlooked. In this connection, the significance of hematuria is re-emphasized. Hematuria is not associated with early prostatic hypertrophy; its occurrence calls for a thorough investigation of its cause.

FIGURE 1 (d)
Wilms' Tumor—*Postoperative View of Patient*

Same patient—After surgical removal of tumor.
(Courtesy of E. A. Ullmann, M. D., Chief of Tumor Clinic, Michael Reese Hospital, Chicago)

Cystoscopy is the essential and most reliable diagnostic measure. It should be done at the very earliest indication. Biopsy is necessary only where inspection leads to inconclusive results.

THE TESTICLE

Testicular tumors are not common, but **most of those encountered are cancerous.** Furthermore, they are usually fatal because the early signs and symptoms are not attention-compelling and because palpation of the testes too often is not done in the course of routine physical examination. Testicular cancer has an early age incidence, usually appearing between the ages of 25 and 45 years.

Symptomatology and Diagnosis

Painless enlargement of one testis is usually the first manifestation. So long as the tumor is confined within the tunica albuginea, the shape and contour of the gland remains unchanged. The initial enlargement may come to an early standstill, remaining this way for weeks or years, then take a rapidly progressive and malignant turn.

Pain and tenderness are less frequent early symptoms, but a dragging sensation is often experienced. **Hydrocele** of a minor degree, a common occurrence, will not transmit light. It should not be tapped unless quite necessary for palpation of the testicle.

The **consistency** of the gland—whether enlarged or not—is hard but not necessarily stony. The rarely encountered choriocarcinoma is an exception in that it is a soft tumor.

There are no **palpable lymph glands** except in the later stages.

Differential diagnosis between gumma, cancer, and long-standing hydrocele or hematocele may be difficult. If there is a suspicion of cancer, **biopsy is contraindicated;** surgical removal is far safer.

A positive test (Aschheim-Zondek, or Friedman) for **anterior pituitary-like hormone**—Prolan A—in the urine or exudate from a hydrocele, is indicative of a testicular tumor; it never occurs in the urine of a normal male. A negative test, however, does not exclude the possibility of cancer.

Early diagnosis and early treatment of cancer of the testicle will usually bring about a cure. Adequate treatment requires both surgical removal of the testicle and follow-up irradiation.

THE PENIS

Cancer of the glans penis affords an excellent example of the carcinogenetic properties of chronic irritation. It is almost always associated with phimosis, and virtually never found in the circumcised.

Not only does phimosis promote penile cancer, but it also conceals the early lesion when it is still in the stage of painless vegetation or of a small erosion or ulcer. This indicates the **prophylactic value of circumcision in infancy;** in later life its value is dubious. Following this operation in an adult, if the incision line fails to heal properly and shows repeated crust formation it should be viewed with suspicion. Cancer may be the interfering factor.

The **cancer** may cause secondary manifestations, such as balanoposthitis, lymphangitis, adenitis. Inasmuch as the primary and causative lesion may be concealed behind a phimotic and redundant prepuce, thorough exposure of the glans for inspection and palpation is imperative; there should be no hesitancy about performing a dorsal slit operation in order to accomplish this.

The **indurated area of the ulcer** may be confused with a luetic ulcer, tuberculous ulcer, a simple wart, or a chancroid. When there is the slightest doubt biopsy should be performed, because the ulcerating, infiltrative type of cancer has a tendency to spread rapidly.

The **superficial inguinal lymph nodes** may show hyperplasia at an early stage. These drain the skin and subcutaneous tissues of the penis, while the glans and urethra drain into the deep inguinal and external iliac nodes of the pelvis. There is an anatomic connection between the two groups. A lesion on one side of the penis may produce metastases in the inguinal glands of the opposite side.

Leukoplakia and **erythroplasia** of the glans penis are considered to be precancerous lesions. The red patches of erythroplasia may be single or multiple, are clearly delineated, are not undermined and not indurated.

Carcinoma of the penis is usually located on the glans or the coronal sulcus.

Bowen's disease, a precancerous dermatosis, may occur on the glans as single or multiple conglomerate papules or nodules with rolled borders. It may resemble erythroplasia or Paget's disease.

Paget's disease is found on the shaft of the penis. It begins as a small patch which, in the course of years, ulcerates. The margin of the ulcer is sharp and red in color; the borders are not rolled; the surface has a finely granular appearance.

The prospect for complete cure of penile cancer is excellent when the diagnosis is made early.

THE PROSTATE

It has been estimated that about 20 per cent, or one-fifth, of all males past the age of 50 years harbor cancer of the prostate. This reported percentage is so high that it certainly behooves every physician to keep the point in mind every time he examines a middle-aged or elderly patient for any cause.

As in ovarian cancer, cancer of the prostate is far advanced before symptoms become so distinct or distressing that they arrest the attention of the patient or his physician.

Early prostatic cancer is discoverable only as an incidental finding in routine rectal examination of males beyond the age of 44 years. This re-emphasizes the great importance of never neglecting to **explore the rectum in routine examinations** of middle-aged or elderly men.

The age of highest incidence for prostatic cancer coincides with that for benign prostatic hypertrophy (hyperplasia), the two conditions appearing concurrently in a high percentage of cases. This is fortunate in many instances, because the benign hypertrophy often produces symptoms of urinary obstruction, while the cancer is still in its early, symptomless stage. The cancer may thus be discovered incidental to the examination and treatment of the hypertrophic gland.

Symptomatology and Diagnosis

The most common primary site for prostatic cancer is the posterior lobe which is also the portion of the gland most easily palpated by the examining finger in the rectum; whereas, prostatic hypertrophy (hyperplasia) usually begins in the lateral and median lobes which are not so readily felt.

The cancer is first felt as a solitary nodule of stony hardness. Later, the gland becomes irregularly enlarged, stonily indurated, and fixed to the surrounding tissues.

The first subjective symptoms are usually urinary frequency and burning micturition. These are not

early symptoms, it must be remembered. There may also be some difficulty in passing the urine.

The diagnosis of early cancer of the prostate practically never requires more than digital palpation. **When the finger has found the evidence,** nothing is to be gained by cystoscopy.

Radical surgical removal of the prostate in the early stage of cancer is almost uniformly successful in bringing about a cure.

Serum Phosphatase—A few words may be added regarding the significance of serum phosphatase and its determination. The fact that its elevation may indicate bony metastasis of prostatic cancer does not make phosphatase determination a method for diagnosing early cancer, although phosphatase elevation may be one of the earliest signs. Let it be repeated that in spite of bony metastasis, eradication of the cancer may yet be possible!

There are two clinically important types of phosphatase occurring in serum (hemolysis-free): An **alkaline** phosphatase with optimal activity at about pH 9.3, and an **acid** phosphatase with optimal activity at about pH 5.

Alkaline phosphatase is found in ossifying cartilage, in bone, and in many other tissues as well. Its increase beyond the normal level appears to be associated with increased osteoblastic activity. While an increase thus accompanies osteoblastic metastases more pronouncedly than osteoclastic metastases, this relation is not invariable.

Acid phosphatase, however, is not related to any specific osteoblastic activity, but is strictly tissue-specific in that it is typical of the prostate and of metastases from prostatic carcinoma.

Hence, the importance of having both types of phosphatase determined.

While elevation of alkaline phosphatase is highly nonspecific and may indicate any of a number of diseases involving bone (such as Paget's disease, osteogenic sarcoma, carcinomatous metastasis, etc.) the additional finding of an elevated acid phosphatase level establishes the diagnosis of bony metastasis of prostatic cancer. **No other disease is known to show a concurrent elevation of both types of phosphatase.**

Determination of phosphatase is also of value in any instance of contemplated surgery on a carcinomatous prostate, in order to determine the presence of bony metastases which may have escaped clinical or roentgenologic examination.

Benign Today—Malignant Tomorrow

The word "precancerous" is not a meaningless term. So-called precancerous lesions, although not always clearly definable, always represent a real threat. The preceding CANCER BULLETINS have repeatedly stressed the grave responsibility assumed by the physician who finds a suspicious-looking or "precancerous" growth, even though biopsy disproves the presence of malignant degeneration at the time. Such lesions must be kept under constant observation until and unless they are eradicated or healed.

An interesting coincidence, in connection with a lesion illustrated in a recent BULLETIN, serves to corroborate this contention in a convincing manner. On page 6 of BULLETIN No. 4, Fig. V shows a "Cancerous appearing ectropion, eversion and erosion, proved benign by biopsy." This picture was taken and the negative biopsy was done in 1940. A few days ago a letter was received from the physician who originally submitted the illustration and case history. We will quote from this letter:

> "You will be interested to know that the colored plate which I furnished you of a cancerous-appearing ectropion, eversion and erosion which was benign in 1940, has now turned up in my office as an early carcinoma. I advised this patient six years ago to have a vaginal hysterectomy. . . . Three years ago while visiting her family in Wisconsin, a local doctor in her home town cauterized her cervix thoroughly, but did not repair or advise hysterectomy. . . . The cervix had healed every place from the cauterization except one area from 6 to 9 o'clock. The surface was raw, the edges a little raised and so I took a biopsy in my office and the report came back 'early carcinoma.' I had removed practically the whole carcinoma in my biopsy because when I took her to the hospital and cut away the entire area, we found only small pieces of malignant tissue. She was given 4400 mg. hours of radium and left the hospital the day before yesterday."

Here is an example of what alertness on the part of the physician can accomplish. This physician disproved cancer in a suspicious-looking cervix, by biopsy, in 1940—six years hence. He did not see her again until a short time ago. She had recently been pronounced "perfectly all right" by someone in a hospital clinic. She had undergone cervical cauterization three years ago, and the cervix looked "all right" to this physician also, except in one small area. He did not rely on the biopsy finding of six years ago, but repeated the biopsy and found a very early cancer which was amenable to surgical extirpation. This patient is probably "cured" of her cancer.

Assuredly, suspicion backed by positive action is an excellent thing—even when faced by contrary opinion—when it can accomplish a life-saving result. And certainly, repeated examinations and continued observation are imperative in the presence of a suspicious-looking lesion.

CANCER BULLETIN No. 7 will contain an article on "Early Diagnosis of Tumors of the Brain and Spinal Cord" and another on "Early Diagnosis of Cancer of the Skin and Lip, Liver, Gallbladder, and Pancreas."

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. 1 NO. 7

EARLY DIAGNOSIS OF TUMORS OF THE BRAIN AND SPINAL CORD

The clinical diagnosis of primary malignant tumors of the brain and spinal cord resolves itself primarily to the diagnosis of **tumor** without regard to type. A preoperative diagnosis of cancer cannot always be made, even after the diagnosis of tumor has been established.

Primary cancer of the brain and cord is supposedly rare. Table I of BULLETIN No. 2 shows the incidence of cancer deaths as 1.6%, the lowest in this table. But it must be remembered that this table shows cancer mortality statistics only. Fortunately, a number of primary cancers of the brain are recognized and surgically removed before they are allowed to cause death. Hence, cancer of the nervous system is not so rare as it may seem.

BRAIN TUMORS

Unfortunately—as, perhaps, is to be expected—the early diagnosis of brain tumor is still all too rare an occurrence. This can be explained by the many and real difficulties involved in arriving at such a diagnosis; it frequently requires all the skill and ingenuity of a specialist in this field.

Inasmuch as most patients consult a **general practitioner** first, it may be well to formulate the part he should play. First, it is he who **should primarily suspect the possibility of a brain tumor,** search for further evidence on which to base his suspicion, and then consult a specialist for verification or negation. Second, even though he feels quite positive of the diagnosis of tumor, he needs the aid of a neurologic specialist to determine its nature and to classify it. It is too "tricky" a field for any except those who devote their entire time and attention to such a specialty.

Symptomatology

There are a few outstanding symptoms which should immediately arouse suspicion of brain tumor:

In infancy—enlargement of the head
In children—vomiting without apparent cause
In adults—repeated cerebral insults, recurrent headache, epilepsy
In all ages—failing vision

Vomiting due to intracranial tumor usually is of the intermittent type. It is differentiated from the so-called cyclic or intermittent vomiting by the fact that after an attack of vomiting due to a tumor the child may be fed as if nothing had happened, whereas in cyclic vomiting this is not true, and nutritional impairment follows. Furthermore, when vomiting results from a tumor, abdominal distress and pain are usually absent, and the vomiting is often projectile in type and without preceding nausea. **No reliance, however, can be placed on absence of nausea or projectile vomiting.**

Headache is such a frequent complaint, and so often due to trivial and passing conditions, that its potential significance may be overlooked — unless every complaint of headache is regarded seriously by the physician.

Headache caused by brain tumor may be constant or it may be intermittent, occurring in the form of prolonged attacks. In the latter instance, it **may be mistaken for migraine** and be treated on this basis, resulting sometimes in a long delayed diagnosis. Any patient with more or less severe headaches which have begun in adult life (after the age of 30), not caused by chronic sinusitis and without the hereditary background of migraine, should have the benefit of an **ophthalmoscopic examination**

and consultation with a neurologist. Even though seen at a stage too early for a diagnosis, persistence of the headache makes it imperative that the patient be frequently observed and checked. Thus, early evidences of tumor may later be detected.

Epileptic seizures may be due to brain tumor, and are readily mistaken for idiopathic epilepsy. Even when a tumor is the underlying cause, the seizure may be manifested as a general convulsion without revealing any sign of a focal character.

The age incidence is of some value in heightening suspicion. In idiopathic epilepsy, the first seizure occurs before the age of 15 in 50% of cases; before 30 in 85%; and before 40 in more than 90%. The more common causes of epileptic seizures in adult life are cerebral arteriosclerosis, cerebral syphilis, or brain tumor. The responsibility for determining which etiologic factor is the present cause should be shared with a specialist.

A feeling of **giddiness** is a frequent complaint in any type of brain tumor, regardless of site. The patient often has difficulty in describing this sensation, and should be aided by helpful questioning. Is it present when at rest? Is it provoked by change of position, especially when quickly made? Is it accompanied by nausea or increase in the headache? Does it take the form of vertigo?

Paresis of the 6th cranial nerve (the abducens) is always a suggestive symptom. Its course below the pons makes it particularly vulnerable to increased intracranial pressure.

Pressure on the scalp may evoke localized pain when the dura mater or skull is involved.

Two symptoms of prime importance are **mental deterioration and personality change.** Intellectual deterioration, it appears, must reach an amazingly high degree in many instances before being noticed by family and associates. Hence, a much more delicate indicator of derangement is alteration in social attitude: The patient becomes quarrelsome at home and is unable to get along with fellow workers. Under such circumstances, the physician should first allow a neurologist to exhaust all methods of diagnosis for organic disease before yielding to the temptation to treat the patient on psychosomatic grounds.

What Should Not Be Done

There are certain procedures that should not be attempted, where brain tumor is suspected, except by competent specialists. The difficulties are so consummate that the diagnostic armamentarium of several specialties may be required.

Extreme **caution is necessary in the administration of narcotics, particularly morphine,** because sudden death not infrequently follows their use.

Spinal puncture should not be done by anyone who has not had special experience with it. It is dangerous, and may even prove fatal.

With the exception of x-ray films of the sella turcica, requests for films of the skull and for encephalography or ventriculography should be reserved for the neurologist or neurosurgeon. Such roentgenography entails great inconvenience; it is always painful; and encephalography and ventriculography are not without a definite mortality risk.

TUMORS OF THE SPINAL CORD

Intramedullary tumors of the spinal cord give rise to a neurologic syndrome characteristic of involvement of the central gray matter. Perception of pain and temperature are lost at the level of the involvement, whereas those of touch and vibration are unimpaired. From the patient's viewpoint, loss of pain and temperature perception are usually no cause for complaint, so that he will not call the physician's attention to these symptoms. They are likely to be discovered only if it becomes routinely part of every first examination to scratch with a pin over the patient's entire back and over his chest and abdomen. This simple procedure is of value, apart from tumor diagnosis, in revealing zones of hyperesthesia (Head's zones) or hypo-esthesia.

Extramedullary tumors produce a **radicular syndrome,** by irritating either the motor or sensory roots first, depending upon the site of the tumor. **Early motor symptoms** are local twitching or fibrillation; these manifestations may be extremely fleeting, invisible during examination. On the other hand, shivering may simulate fibrillation.

Much more easily recognizable is sensory radicular irritation. **Neuralgic pains** are fortunately the rule in early extramedullary growth. Pain is intermittent, intense, lancinating; it may last only a few seconds, but does not lead, in spite of its intensity, to pain on deep pressure or to pain along the nerve trunks. In the area of pain attacks, a superficial skin hyperesthesia may develop, of such intensity that the patient may react out of proportion to the needle-scratch test in this area.

Again it should be emphasized that when there is any reason to suspect a cord tumor the patient should have the benefit of a neurologic consultation. Cord tumors, like brain tumors, are not simple to diagnose, localize, or differentiate.

EARLY DIAGNOSIS OF CANCER OF THE SKIN AND LIP, LIVER, GALLBLADDER, AND PANCREAS

Malignant lesions of the skin and lip are not too difficult to apprehend, but cancer of the liver, gallbladder, and pancreas present problems which may, at times, seem insurmountable.

But this does not lessen—rather, it increases—the responsibility of the physician in whom the patient places his confidence. **Alertness, awareness, and seizing every straw of symptomatic significance** may spell the difference between early diagnosis and missed diagnosis—between life and death. Our one great hope is that we may arouse the inquisitive and suspicious attitude of the physician, so that when a leading symptom or sign is present, no matter how unimportant it may seem at the time, it will not be overlooked or by-passed until its actual significance has been determined. Therein lies the principal hope for success in the campaign to reduce cancer mortality.

THE SKIN

Affections of the skin are annoying, even if not painful, to a patient, and for the most part visible to him. Cancerous skin lesions are mostly curable in their early stages, are often preceded by precancerous conditions, and frequently reported to a physician or seen by him during the course of an examination. In spite of this, **the reported mortality rate** of this readily seen and not too difficultly diagnosable form of cancer **is appallingly high**—more than 5% of cancer deaths are due to cancer of the skin, including the lip.

The visibility, the warning signals of precancerous lesions, the usually slow growth, the amenability to treatment in the early stage—propitious features of skin cancer—are largely nullified by wrong diagnosis, neglected diagnosis, or misjudgment as to the malignant potentiality of the affection seen. Time—precious time—is then lost through inadequate or wrong treatment or no treatment.

Inadequate treatment, indeed, involves even more than mere delay: The irritation it produces may actually spur the malignant lesion to more rapid growth and development. In order to circumvent this danger, a good rule to follow is this: When an apparently benign, circumscribed skin lesion shows no response after two weeks of treatment, steps should be taken to insure an *accurate* diagnosis. The important step in such a case is **biopsy.**

Keratosis Senilis

Senile keratosis is a harsh, dry state of the skin which appears in old age. The keratotic areas are circumscribed, forming varicose or flat islands on the skin. Sometimes the growth resembles filiform warts; at other times it forms thin laminae of scales which bleed when peeled off.

Senile keratosis represents **a precancerous lesion.** Threatened malignant change is indicated by an increased rate of growth, rather than by actual

FIGURE I

Skin Cancer?

Circumscribed hyperkeratosis in middle aged patients should arouse suspicion of cancer
(Courtesy of *What's New*, March 1936)

changes in the tissues of which it is composed. It appears, as a rule, in old age, and characteristically develops on parts exposed to the sunlight and the open air. The keratotic patches are usually more brown or pink than the surrounding skin.

This dermatosis should be kept under careful and continuous observation, particularly when the base is inflamed and surrounded by a belt of hyperemia. Such a development indicates a tendency to an increased rate of development.

Special Types of Skin Cancer

Basal Cell Carcinoma (epithelioma, rodent ulcer)—This type of cancer develops from the basal cells, the deepest layer of the superficial epithelium, and retains the character of these cells. There are two forms to consider—the **superficial** variety, and the **deep** and nodular, papillomatous or fungoid tumors.

a) **Superficial epithelioma**—This type of cancer not infrequently develops in a patch of senile keratosis—on the face, in the ears, on the skin of the hands, and on other exposed areas. The first indications are thickening of the keratotic patch and slight redness. Removal of the crust uncovers a superficial granulating ulcer which expands slowly in area.

The epithelioma may also originate from a seborrheic keratosis.

When basal cell carcinoma develops in an otherwise intact skin area, it appears in the early stage

FIGURE II

Basal Cell Carcinoma

Small, waxy elevation representing the first phase.
(Courtesy of *What's New*, March 1936)

as a small whitish, yellowish, or pinkish nodule of waxy translucency. No symptoms are noted until ulceration begins. There may be a single nodule or several; when multiple, they may be scattered singly or be grouped. **The consistency of the nodule is not diagnostic.**

The nodules may undergo no significant change for years, or they may be destroyed by ulceration and new nodules appear. Spreading ulcers develop beneath the crust; their increase in size may cause profound destruction, particularly in the face about the nose and orbits. The destruction is one of contiguity, however, since metastases are almost never encountered.

A sign which should arouse suspicion of the cancerous character of this new growth is the presence of **dilated blood vessels** on the surface or at the periphery of the nodule.

Another type of rodent ulcer, inflammatory in character and with crust formation, resembles Paget's disease of the breast.

b) **Deep epithelioma**—This type of basal cell carcinoma is far more dangerous than the superficial type. It may be deep-seated from the start or it may evolve from the superficial form. The nodules are embedded within the skin layers, below the superficial layer, and are not elevated. Later, they form flat plaques with irregular contours. Telangiectatic blood vessels covering the surface give them a red appearance.

Sooner or later, the affected area ulcerates, **rapid extension takes place** (both in depth and in superficial area), the lymphatic system becomes involved, and generalized metastases lead to a fatal termination.

Epithelioma of the Lip—Cancer of the lip seems to be intimately associated with chronic irritation of one sort or another. The **causes** for such irritation may be negligence in oral hygiene, countlessly repeated episodes of pressure plus heat from pipe stems, chemical agents (such as tarred threads held between the lips by shoemakers at work), or even ultraviolet radiation from sunlight.

Lip cancer has a **predilection for the mole and for the lower lip.** This predilection for the lower lip (98%, of the time) is indeed fortunate, because cancer of the upper lip is usually much more malignant.

The lesion appears first as a small nodule, a keratotic patch, an insignificant looking lissure, or a tiny abrasion such as may result from a razor cut. Fissures and minor injuries heal quickly and spontaneously, but the cancerous lesion does not, nor does it respond to usual therapeutic measures. This observation alone—its **refractoriness**—should arouse suspicion.

A slowly expanding ulceration follows. From its gross appearance, a full-blown ulcer is most often confused with a chancre or syphilitic ulcer. Inasmuch as a syphilitic patient may also have cancer, **biopsy is imperative,** to clinch the diagnosis. Positive serologic and darkfield examinations do not rule out the possibility of cancer.

The probability for cure is closely related to the size of the ulcerated area. The larger it is, the poorer the prognosis. Hence, **early diagnosis** which carries with it a **90% probability for cure,** is essential. But, even when the regional lymph nodes are invaded, the condition should not be regarded as hopeless, there still remains a 50% probability for cure under adequate treatment.

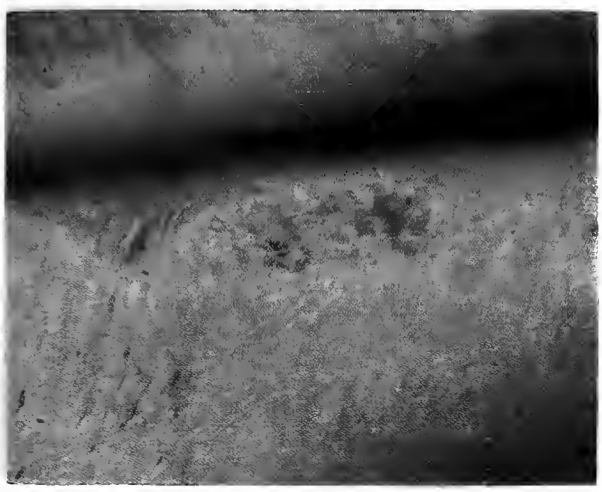
Reference to Fig. II in BULLETIN No. 2 will show that the regional lymph nodes for the upper lip are the inframaxillaries, for the lower lip, the inframaxillaries and submental. The drainage into the submental nodes is contralateral as well as homolateral, so that metastases may be found on either side or both sides.

Squamous Cell Carcinoma (epidermoid)—This type of cancer develops from the squamous epithelium with cuboid cells; it is much **more malignant than the basal cell carcinoma.** Whereas basal cell carcinoma is frequently a slow-growing tumor which destroys tissue by expansile ulceration (excepting the rarer, deep-seated, locally metastasizing variety), squamous cell carcinoma tends to metastasize early.

It is an insidious growth, first noted as a small, papillomatous or verrucous papule, or as a small, well defined nodule of a yellowish or reddish tint, with a central horny spike. Within a few months it begins to ulcerate, while the new growth expands peripherally and its edges become undermined. A clinical diagnosis derived from the history and inspection of the lesion is not to be relied upon.

FIGURE III

Cancer of Lower Lip



Small ulcer, frequently cut during shaving, may be an early carcinoma (epithelioma
(Courtesy of *What's New*, March 1946)

Biopsy should precede treatment of a lesion of this description, in order to avoid delay in the application of proper and adequate therapy.

Melanoma (malignant nevus-cell tumor) — The term "melanoma" is variously defined. By some it is used to indicate any tumor made up of melanin-pigmented cells; by others it is limited to melanotic tumors of a malignant character. Probably every melanoma is at least potentially cancerous, and for the purposes of this discussion, melanoma will be regarded as a malignant tumor.

The new growth usually originates in a pigmented nevus of the skin, most often on the extremities or on the face. A hairy nevus almost never gives rise to a melanoma.

Although relatively few ever show cancerous changes, **every pigmented nevus is potentially dangerous.** Trauma and irritation seem to be important factors in the transmutation of an apparently harmless mole into a malignant melanoma. Hence, from the prophylactic standpoint, wide excision of pigmented moles, before puberty, should always be considered carefully when they appear on areas exposed to frequent or chronic irritation, such as the palms, soles, anorectal area or genital organs. In the adult, **these nevi should definitely be excised** if they show any changes due to irritation, such as increase in size or intensification of pigmentation.

The degree of pigmentation is not in itself, however, a gauge for determining the cancerous potentiality of a nevus. Therefore, it is safer to excise widely all elevated nevi, whether deeply pigmented, slightly pigmented, or unpigmented (white moles or amelanotic nevi). If an excised mole shows cancerous changes on microscopic examination, the question arises whether the regional lymph nodes have been invaded.

An exception must be made of the so-called blue nevus: Prophylactic excision carries with it a high and unpredictable mortality risk. This nevus exhibits a blue-gray or blue-black discoloration, is elevated slightly above the surrounding skin level, has a firm consistency, and is round or oval in

FIGURE IV

Pigmented Nevus

Kerototic pigmented nevus of right breast.
(Courtesy of E. A. Uhlmann, M.D., Michael Reese Hospital, Chicago)

shape. The usual sites for the blue nevus are the face and the dorsum of the hand or foot.

Although a blue nevus should not be excised merely as a prophylactic measure, excision may become necessary in the presence of irritative changes and growth. In such a case, **irradiation should precede excision,** since irradiation appears to reduce the risk.

The end-result of malignant changes in a blue nevus is **melanosarcoma,** a highly malignant disease. For this reason accurate and frequent observations of such nevi should be insisted upon by the physician and the patient should be informed of the dangerous potentialities, so that he will inform the physician promptly of any changes noted.

THE LIVER AND GALLBLADDER

In the present state of our knowledge there is little to be said about early diagnosis of primary cancer

of the liver and gallbladder. Early diagnoses are practically never made, because there are no signs, symptoms, or diagnostic methods to indicate the presence of cancer in an early stage. In attempting to differentiate between cancer and cirrhosis of the liver, before resorting to exploratory laparotomy, **peritoneoscopy** may prove of decisive value.

Fortunately, primary cancer of the liver is relatively rare in the United States. The incidence is much higher abroad among certain groups of Orientals and Africans. Even in this country, the highest incidence is among our Negro population.

Primary liver cancer in an early stage—such as the solitary adenoma—may be amenable to surgical extirpation. Should such a neoplasm be discovered, it should be removed, to **give the patient a chance.**

Primary cancer of the gallbladder is one of the most malignant forms of cancer. Early diagnosis—even though possible or when established by accident—is of little avail. Even early diagnosis is apt to be too late. Prophylaxis seems to offer the best chance.

The **only prophylactic method** of any value consists in the surgical extirpation of gallbladders which are known to harbor stones. It is known that cancer occurs more frequently in the presence of cholelithiasis than in normal gallbladders.

THE PANCREAS

The age incidence for primary cancer of the pancreas is about the same as that for cancer of the stomach. The male is afflicted more often than the female.

Early recognition of pancreatic cancer may offer formidable difficulties. Traditional teaching has emphasized painless jaundice as a chief sign, but **many patients are not jaundiced** when they first consult a physician in connection with their complaints.

The **principal early complaint** is epigastric pain which radiates to the middle of the back, a **pain** which progresses in intensity as time passes. Inasmuch as this pain is frequently and erroneously attributed to the vertebral column or muscles of the back, the paradoxical relationship between it and body positions is noteworthy: The pain increases on lying down, and at least some measure of relief is gained by sitting up or, better still, by bending forward. There is no relationship between pancreatic pain and eating or defecation—a point for differentiating it from pain of hepatic or gastrointestinal origin.

Occasionally, gross **hemorrhage** from the intestines, for which no gastric or intestinal basis can be found, will indicate a penetrating pancreatic carcinoma.

Concurrence of **fever** without apparent cause—frequently encountered in pancreatic cancer—and gastrointestinal complaints of obscure origin should arouse suspicion.

Laboratory analyses offer no typical findings. **Fatty stools and abnormal carbohydrate metabolism are only rarely encountered.** Occult blood may be demonstrated, but this may result from any of many causes.

A highly suggestive sign is elicited by a combination of roentgenography, fluoroscopy, and palpation. If the sweep of the duodenum is wider than usual, and cannot be deformed by palpation, it points to the head of the pancreas as the cause of the widening. In this way, carcinoma of the head of the pancreas may be discovered in a relatively early stage.

When carcinoma of the head of the pancreas interferes with the flow of bile into the duodenum, the ensuing jaundice is frequently accompanied by pain.

Courvoisier's law—a gallbladder much distended from obstruction of the common duct indicates tumor rather than calculus—applies here. If there is clinical evidence of obstructive jaundice and a distended gallbladder, the diagnosis of cancer is practically certain.

Loss of appetite and weight loss are later symptoms. Indigestion, nausea and vomiting, constipation and diarrhea are symptoms which occur but are common to so many other conditions that they have no diagnostic value.

There are **no physical findings in the early stage.** If the tumor is palpable, it is in an advanced stage.

In most instances, when signs and symptoms are suggestive, exploratory laparotomy is indicated in order to clarify the diagnosis.

ANOTHER GLIMPSE INTO FUTURE ISSUES

The next issue of THE CANCER BULLETIN (Vol. I, No. 8) will conclude the series of *general* articles on early diagnosis of cancer with an article on cancer of the bone. For these articles, many sources have been consulted to compile, pool, and condense such information as might seem practical and useful. An effort has been made to present pertinent facts and information only, and to avoid controversial issues.

The presentations to follow, for completion of Volume I (12 BULLETINS), will be based on material supplied by qualified specialists in various fields. These will naturally give the subjects more exhaustive treatment than was possible in the more comprehensive discussions preceding them.

The first of these *special* articles—on the value of roentgenology in cancer diagnosis—will begin in the next issue. Anticipated treatises will deal with the specialist's approach to diagnosis by pathologic examination and by endoscopic methods—gastroscopy, bronchoscopy, proctoscopy, and cystoscopy.

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 8

EARLY DIAGNOSIS OF CANCER OF THE BONE

Early diagnosis of bone cancer is not a simple matter. These tumors occur but rarely and are even more rarely recognized in their incipiency. Correct early diagnosis, when accomplished, most often results from collaboration between the clinician, surgeon, roentgenologist, and pathologist.

No single feature—clinical, laboratory, or roentgenographic—is sufficiently typical to differentiate definitely between benign and malignant affections of the bone in an early stage. Even histologic examination of **biopsy** material, a diagnostic method of outstanding importance, **is more difficult and less often applicable** in the differential diagnosis of bone tumor than in most other conditions in which it is used. Hence, it is **imperative,** whenever a bony disease is present or suspected, to go into the history in the minutest detail, to do the general physical examination in a most complete and thorough manner, and to have extensive roentgenographic studies made.

X-ray

The roentgenologist should be informed when there is a suspicion of a bone disease, and the **extent of the x-ray examination** should then be left entirely to his discretion. It is frequently necessary to make films of other bones (particularly corresponding bones of the opposite side) for comparison; also, to obtain views in various planes. The x-ray examination cannot substitute for a competent physical examination; it is a **supplementary study** which should follow, not precede, the other.

The changes in the bone or periosteum may be so slight that they would not be discovered in a routine x-ray examination; whereas, if the attention is focused on a clinically predetermined area the pathologic process may become noticeable.

The radiologist should be looked upon as a clinician, interested in the investigation of disease by a special method, and not as a photographer of specified or unspecified parts of the human body. Only in this way can we achieve the maximum aid that radiology has to offer in the early diagnosis of cancer.

Repeated examinations are important—even imperative—when, in the face of suspicion, the first examination does not yield definite results. Subsequent examinations, by comparison, will indicate whether there is any growth or extension of the process.

Syphilis

Syphilis, the great imitator, so protean in its manifestations, must always be considered in differential diagnosis. Neither history nor age can rule out syphilis; serologic tests are essential. Again, however, it must be remembered that syphilis and cancer may co-exist.

Biopsy

Some authorities advise biopsy and frozen sections whenever possible, in order to enable the surgeon to proceed at once with treatment based on the pathologist's report. When frozen sections are not feasible, or when an expert pathologist is not available, roentgen studies must form the basis for procedure. Other authorities, however, contend that, when x-ray studies are inconclusive, additional information of value is seldom yielded by biopsy.

An untoward influence in biopsy of bone may be exerted by excision of multiple specimens from different sectors of the affected part for all-inclusive sampling. **It may lead to acceleration of the tumor growth,** as well as to diminution of the strength of the bone.

The histologic picture presented by **normal callus formation** is often so difficult to distinguish from that of sarcoma—even by specialists in this field—that the risk of making an erroneous diagnosis is great. If the biopsy report is used as the criterion for determining therapeutic procedure, an **erroneous diagnosis of sarcoma** may lead to the unnecessary performance of a mutilating amputation.

In malignant myeloid sarcoma (osteoclastoma) which is amenable to x-ray treatment, removal of bone tissue for biopsy may be equivalent to the removal of the scaffolding on which the repair is dependent. Thus, the diagnostic procedure will nullify the chances for recovery.

If, in spite of its limitations, biopsy appears desirable, the surgeon should be supplied with the films showing the exact location of the lesion, and the projection of the lesion should be clearly marked on the patient's skin before the operation is undertaken.

Trauma and Cancer

The theory that a relationship exists between trauma and the origin of cancer of the bone is now quite generally discredited. The **coincidence of trauma and subsequent discovery of a bone cancer,** however, plays an important role in medical practice, and particularly in the minds of patients.

Many patients with bone disease volunteer the information that an injury previously suffered marked the beginning of their trouble. It is important, therefore, following any trauma, that the patient be given the benefit of an x-ray examination of the part as soon as possible after the injury. The time and type of trauma should be accurately recorded along with the reports of the x-ray examination.

An experienced roentgenologist can judge, with a high degree of accuracy, whether an existing lesion followed traumatization or was existent before the trauma was incurred. A silent, previously existent lesion of the bone may be activated by injury, so that the patient's conclusion, that the trauma was the causative factor, is only natural.

In this connection, special attention is called to **the diagnostic implications of fracture.** A bone weakened by neoplastic infiltration may be fractured by even a **slight** injury—the so-called "pathologic fracture." Such a fracture is likely to arouse the physician's inquisitive interest, and lead to deeper investigation. On the other hand, if a similarly affected bone is fractured as a result of a **severe** injury, the underlying bone pathology may not be suspected, and a **cancerous tumor may escape attention**—unless special consideration is given to the exhibition of any deviation from the usual clinical manifestations of fracture, such as abnormally diminished or abnormally intense and lasting pain.

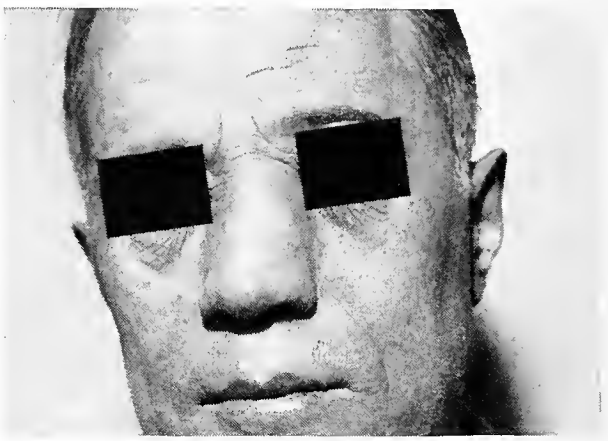
If a lesion has been roentgenographically visualized and identified as having resulted from traumatization, differentiation between a simple inflammatory reaction to the trauma and a newgrowth can be made only by **repeated x-ray examinations** to show regression or progression.

It is unquestionably true that sarcoma does rarely develop at the site of an old fracture. **Early diagnosis** of such a complication depends upon comparative studies of recent x-ray findings (when the patient first complains of subjective or objective changes in the involved area) and previous films of the fracture (taken after healing has reached the final stage of consolidation). This serves to re-emphasize the necessity for making and keeping complete x-ray records of fractures and bone injuries; films should be made early, repeatedly, and adequately, to cover every phase of the injury and its repair.

Sarcoma

Most cases of primary cancer of bone fall under the general classification of sarcoma, which is subdivided into osteogenic sarcoma, chondrosarcoma, fibrosarcoma, and Ewing's tumor (endothelial myeloma).

Sarcoma of Nose



The newgrowth is of periosteal origin.
(Courtesy of E. A. Uhlmann, M. D., Tumor Clinic, Michael Reese Hospital, Chicago)

Sarcoma is most often encountered in young patients. The femur is the most common site. The incidence is higher in males.

Pain

Pain is an early symptom in sarcoma of the bone, but not invariably experienced. There is no identifying feature connected with the pain. It may be no more than a feeling of "something wrong" or may be intense. It is **sometimes mistaken** for rheumatic pain

or the **"growing pain"** of childhood. It may be constant or intermittent, the duration varying from minutes to months.

Mechanical factors may provoke the pain. There is sometimes **a peculiar discrepancy** displayed: Use of the extremity causes pain which continues as long as the use continues, but pressure on the extremity does not elicit pain.

The pain may appear suddenly, accompanied by elevation of temperature, and the condition be confused with osteomyelitis. Sarcomatous degeneration occurs in a small percentage of patients with polyostotic Paget's disease (osteitis deformans in multiple bones), since the osteitis is itself a painful condition, pain loses its value as a signal of cancer.

In **multiple myeloma**—a primary tumor of the marrow—pain is only rarely an early symptom. It may simulate intermittent rheumatic or neuralgic pain, particularly in the lumbar region, or produce a girdle-sensation in the lower thoracic region. The age incidence of Paget's disease and multiple myeloma is highest in the sixth decade, whereas sarcoma occurs rarely after middle life.

Pain is so **often the only early manifestation** of bone cancer that a careful search for the cause of the pain is highly important. Inasmuch as the first manifestation of bone sarcoma often coincides with or follows soon after an injury, a complaint of pain in a bone should be accurately analyzed for cause, following trauma. The trauma should not be accepted as the obvious cause unless sarcoma has been eliminated as a possibility.

Inspection and Palpation

Changes in **the skin** overlying sarcoma of the bone may or may not be present. These changes do not appear as early as pain.

Circulation of blood and lymph in the skin overlying the affected area becomes impaired, particularly when the tumor is one of rapid growth, leading to localized cyanosis; the veins in the area become dilated and prominent. Neither skin nor muscle is adherent to the bone in the incipient stage, but secondary changes, such as necrosis in the cancerous tissue, may produce adhesions.

Palpation often reveals a spindle shaped mass around the shaft of the bone, which does not completely encircle the shaft. Although this feature is quite typical of sarcoma it may be duplicated by non-suppurative osteomyelitis (Garré)

Parchment-like **crackling on pressure** over the tumor may indicate a simple bone cyst or a central giant cell tumor.

Pulsation in the tumor mass, a frequent concomitance in bone cancer, may be felt.

Fluctuation, indicating abscess formation, in the vicinity of a tumor under suspicion practically eliminates sarcoma from consideration. However, if an exploratory puncture or an injection has been previously made in this area, infection with subsequent abscess formation may have occurred, to complicate further the diagnostic problem.

Systemic Reactions

Early sarcoma of the bone may show nothing but local signs of the disease. Systemic signs are usually more or less late ones.

Fever is rare, in contrast to acute osteomyelitis. When encountered, it usually indicates a rapidly growing tumor.

Cachexia may not be observed unless secondary changes, such as ulceration and infection, supervene.

The **blood** shows no characteristic alteration. Anemia sets in eventually, but may be a late sign. In multiple myeloma, the plasma protein level is sometimes raised considerably above normal. Sedimentation rate may be increased.

Serum phosphotase may be increased in osteogenic sarcoma, but this also occurs in Paget's disease and in benign giant cell tumor.

Bence-Jones protein in the urine indicates, but does not prove, the presence of myeloma.

Comment

At present, the average interval between appearance of the first symptom of bone cancer and instituting of surgical or radiologic treatment is from ten to twelve months. This **delay in treatment must be shortened** considerably if mortality is to be reduced. Delay can be reduced only by earlier diagnosis and prompt and adequate treatment after diagnosis. Again, the case rests with the physician. Alertness to possibilities, suspicion aroused by seeming trivialities in history and examination, thorough and systematic examinations, and co-operation with roentgenologist and surgeon will accomplish much.

The patient's understandable fear of a mutilating operation may lead to an irrational and uncooperative attitude. It then becomes incumbent upon the physician to discuss frankly the vital importance of the contemplated surgical procedure. An attempt should be made to ease the mind of the patient by showing that **modern surgery has advanced** to such a degree that safety no longer may require amputation or disarticulation at the high levels formerly deemed necessary; that nowadays only a minimum of bone is removed; and that artificial limbs and supports are so ingeniously contrived as to make existence quite comfortable even after the loss of an extremity.

ROENTGENOLOGY IN THE EARLY DIAGNOSIS OF CANCER

It has been frequently repeated in previous BULLETINS that reduction of cancer mortality depends primarily upon alertness and vigilance, thoroughness and completeness in the conduct of physical examinations, and a suspicious attitude on the part of the physician. It is only after the physician has exercised his own ingenuity and utilized his own diagnostic acumen to the utmost that physical and chemical diagnostic aids should be called upon. When diagnostic aids are used to supplement, not substitute for, the physician's judgment and suspicion they offer invaluable service. **No one diagnostic instrumentality has more widespread and absolute applicability than roentgenologic study of a patient.**

There is one exception to this usual mode of procedure: Mass x-ray examinations of the chest without previous physical examination (particularly in the armed forces of the United States where millions were x-rayed) has really accomplished something in the campaign against tuberculosis. And, incidentally, some early cases of pulmonary cancer have thus been discovered by chance. Some attempts have been made to conduct mass x-ray examinations (fluoroscopic) of the stomach, in an effort to disclose early gastric cancer, before the appearance of symptoms. Up to the present, this effort has not been strikingly successful.

St. John, Swenson, and Harvey (Ann.Surg. *110*:225-231,1914) examined a group of 2,492 men and women over fifty, not suspected of having gastric lesions. Rapid fluoroscopic examination of the stomach was done and the cases divided into those with normal appearing stomachs and those showing some type of abnormality. The latter were studied further. Three malignant tumors were found—two carcinomas and one lymphosarcoma. Reported experience with fluoroscopy alone indicates that not much confidence can be placed in the rapid fluoroscopic examination to which this group of patients was subjected. Mass x-ray examinations of the stomach or bowel are not yet feasible.

However, **x-ray examinations of the stomach** should be made in individuals above the age of fifty who show absence of hydrochloric acid in the stomach or have pernicious anemia; who give a family history of carcinoma, pernicious anemia or hypochlorhydria, or who have already been told that they have a gastric ulcer or a benign polypoid tumor of the stomach. **Fluoroscopic examination for this purpose is not adequate.** The smaller the lesion, the more improbable it is that it will be recognized on fluoroscopic study. The examination must be radiographic (supplemented by fluoroscopy) with "aimed" roentgenograms, so that films may be conserved and exposures be made accurately over the areas and in the angles of projection most desirable for studying the patient.

Basic Criteria in Roentgenologic Diagnosis

The roentgenologic recognition of digestive tube pathology depends upon the recognition of aberrations from normal morphology or function. The lumen of the organ, as visualized by contrast material, may be distorted by a mass; in an earlier stage, there is rigidity and inelasticity of the wall, or the mucosal pattern is disturbed or obliterated; and certain disturbances of function are noted. The contrast meal or clysma constitutes a mold, so to speak, a fluid, ever changing mold of the cavity of the digestive tube, susceptible to study from many angles.

If the stomach or bowel has not been emptied prior to the introduction of the contrast material, the food material or residues occupy a portion of the space which would otherwise be visualized by the opaque material, and the shadow of the lumen will be incomplete or defective. Such an imperfect shadow is spoken of as a "filling defect." Likewise, a tumor arising in the wall of the digestive tube will displace a certain amount of the opaque medium, and cause a filling defect. Such **filling defects constitute the chief evidence of tumor in a hollow organ.**

The character and location of the filling defect permit conclusions to be drawn as to the nature of the tumor, although there are times when it will be impossible to differentiate roentgenologically between a benign and a malignant tumor, or between a true tumor and an inflammatory mass occurring in connection with ulceration and malignant degeneration. In occasional instances the roentgen findings alone will be decisive where macroscopically a differentiation cannot be made.

The roentgenologic recognition of pathology in the digestive tube has been further refined by **study of the mucosal pattern.** A shrinking or convergence of the rugous folds of the stomach, causing a stellate pattern, may betray an ulcerative lesion. In malignant disease the rugous folds may become obliterated. A certain section of the wall of the digestive tube may become indurated and inelastic, as the first hint of malignant infiltration.

Similarly, in the urinary tract, distortion of the renal pelvis or calices, or an obstruction may call

attention to the presence of pathology. In the uterus, a defect in the normal contour of the uterine cavity may indicate a tumor. In the osseous system, changes in thickness or density of the bone may call attention to the presence of disease.

CARCINOMA OF THE ESOPHAGUS

In carcinoma of the esophagus the prime roentgenographic evidence is a filling defect, rarely recognized before obstruction sets in, because the patient, unfortunately, is not x-rayed until obstructive symptoms become apparent. Many failures to recognize carcinoma of the esophagus in an early stage result from failure of the patient to report initial attacks of mild dysphagia, yet dysphagia due to esophageal spasm is the earliest clinical sign, and usually the symptom which, when it becomes pronounced, brings the patient to the roentgenologist.

The **first signs of obstruction** may be due to spasm set up at the level of the early malignant lesion, or just above it, and are observable before there is any actual narrowing of the lumen. This has been noted especially in cases of carcinoma of the lesser curvature of the stomach, involving the cardiac orifice. **Other signs** of esophageal carcinoma are irregularity of lumen with a defect sometimes annular, sometimes lateral, causing a narrowing of the esophagus; dilatation of moderate degree above the lesion; a tumor mass recognizable in the mediastinum in the region of the defect; disturbances of peristalsis due to the obstruction. Under the fluoroscope, esophageal obstruction exhibits a gradual trickle of opaque material through the lumen in contrast to the complete stoppage observed in spasm.

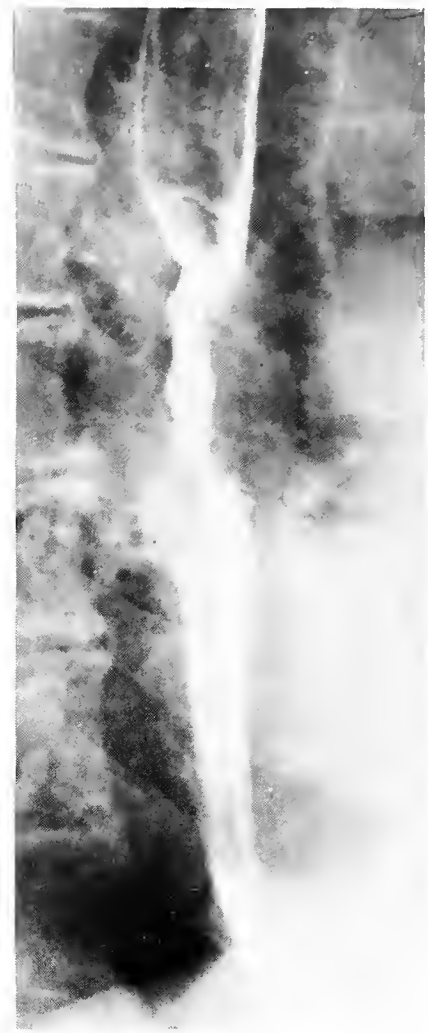
CARCINOMA OF THE STOMACH

Every patient with a complaint of derangement of gastric function (such as anorexia, epigastric discomfort, nausea, or dysphagia) should have a thorough x-ray examination of the stomach. In no other way can the early diagnosis of carcinoma be made. **Normal or even high gastric acidity by no means excludes cancer.**

In general, carcinoma of the stomach is marked by an irregular filling defect; obliteration of the gastric mucous folds (in most cases); loss of elasticity of a portion of the gastric wall; sometimes a palpable mass corresponding to the filling defect; and delay in passage of the contrast meal through the stomach or esophagus if the lesion involves the pyloric or the cardiac end.

Carcinoma of the **cardiac end of the stomach** is often overlooked because of the normal irregularity of its mucous pattern, the normal absence of peristalsis in this part of the stomach, and inability to reach high enough under the ribs to palpate that portion of the stomach. Carcinoma of the cardia

FIGURE I



Carcinoma of the esophagus. Only slightly obstructing; amenable to surgery.

FIGURE II

Carcinoma of the stomach at the fundus. Carcinoma in this situation is very easily overlooked.

may be marked by one or more of the following signs: Irregularity of contour brought out particularly well in the Trendelenberg position; deviation and irregularity of the stream of contrast material as it passes from the esophagus into the stomach; and an increase of the space between the diaphragm and the upper surface of the stomach. Inflation of the fundus of the stomach with air or gas, with study of the patient while in the erect position, further facilitates the recognition of cancer in this area. An effervescent powder may be given to produce the desired gaseous distention of the fundus.

In the **body of the stomach,** adenocarcinoma produces a ragged, irregular defect, with obliteration of the rugae, the defect often showing a punched-out appearance. Scirrhous carcinoma causes a narrowing of the lumen, either unilateral or annular, but with little or no irregularity in the contour of the filling defect. Such a lesion may easily be overlooked, but the chief sign is loss of peristalsis and flexibility of the gastric wall. A polypoid or multinodular type of growth is marked by one or more large, rounded filling defects, with ill defined, irregular edges. This type of lesion may be accentuated by **compression technic:** Make pressure over the stomach with a wooden spoon or loofah sponge while fluoroscoping or radiographing.

Early carcinoma of the **pyloric end of the stomach** may infiltrate the pylorus, causing it to remain constantly open; a more advanced or an annular infiltration may cause it to become funnel shaped. Gastric peristalsis may be greatly increased, although dilatation and hyperperistalsis is not so pronounced as with benign cicatrizing ulcer. Differentiation of a cicatrizing ulcer of the pylorus from scirrhous carcinoma may be very difficult.

Malignant gastric ulcers usually show a niche with a broad base, and a rather large filling defect surrounding it, due to extensive infiltration. Malignant ulcers often present the "meniscus sign," representing a round or half-moon niche, lying within a filling defect. Any ulcer surrounded by a large area of barium-free shadow should be suspected of being malignant.

The surgeon will want all the information obtainable as to the extent of a lesion found, and the surgical possibility for removal. The lesion usually proves to be larger than it appears on the roentgenogram. When the infiltration or defect is in the pyloric third of the stomach, surgical removal is probably possible; in the middle of the stomach, surgical relief is more doubtful; in the upper third of the stomach it is usually futile, although the possibilities for success have been greatly extended by recent advances in surgical methods and postoperative management.

CARCINOMA OF THE DUODENUM

Carcinoma of the duodenum is, fortunately, of rare occurrence, but carcinoma of the pancreas and of the liver is not so infrequent. Duodenal carcinoma most often occurs at the site of the papilla of Vater. It may be recognized as a more or less rounded filling defect in the duodenal shadow, about ten centimeters beyond the pylorus when compression technic is used and the patient is turned so as to bring this portion of the duodenum into unobstructed vision.

In carcinoma of the duodenum there is an **intrinsic** indurative lesion which involves and soon obliterates the mucosal pattern. Invasion of the duodenum by cancer of the head of the pancreas is even more likely to disturb the mucosal pattern and the contours of the duodenum, particularly on the side of the duodenal curve around the head of the pancreas. If the neoplasm has enlarged the head of the pancreas, the duodenal curve will be spread wider than normal. It should be recalled that in large individuals the duodenal curve normally is marked by a larger radius than in small individuals.

CARCINOMA OF THE SMALL INTESTINE

Malignant tumors of the jejunum and ileum are extremely difficult to recognize unless they cause obstruction. Some refinements of technic are now available, from which conclusions may be drawn as to the probable malignancy of obstructive lesions of the small bowel. It may be necessary to introduce a Miller-Abbott tube to the site of obstruction, and instill barium for careful fluoroscopic and spot-film study. Complete visualization of the small bowel may be secured by **fractional administration of the barium meal;** careful fluoroscopy may then enable the roentgenologist to detect the site of the lesion and study its contours. The diagnosis, however, is rarely made early because the patient usually is first seen during an obstructive crisis, when there is neither opportunity nor time for a study of the finer details of the mucosal pattern after locating the probable site of obstruction.

(To be concluded in Bulletin No. 9)

Editor's Note

As indicated in BULLETIN No. 7, the article on cancer of the bone, in this issue, concludes the series of general articles on early diagnosis of cancer.

The *first part* of an article on roentgenography in cancer diagnosis appears in this issue. This article is a comprehensive and detailed description of the role of roentgenographic diagnosis in cancer, which will take up all of BULLETIN No. 9 for its conclusion.

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 9

ROENTGENOLOGY IN THE EARLY DIAGNOSIS OF CANCER

(Concluded)

(Editor's Note: *The first part of this article was published in* BULLETIN No. 8. *It is carried to its conclusion in this issue.)*

CARCINOMA OF THE COLON

Fifteen per cent of all carcinomas encountered are located in the large intestine. About two thirds of these occur after the age of fifty, but quite a number appear before the age of thirty. In younger patients the lesions are characterized by shorter duration of symptoms, a higher index of malignancy, greater frequency of metastases and "inoperability," and a diminished proportion of five-year survivals after treatment.

Accumulating evidence indicates that **most cancers of the colon have their origin in polypoid growths.** Early diagnosis and prevention of colonic cancer may therefore be facilitated by recognition of polyps before they have had time to undergo malignant degeneration or while the degenerative change is still in an early stage of development. All colonic tumors should be treated as malignant growths, because biopsy alone can determine their nature.

The roentgenologic detection of colonic cancer depends upon visualized alterations of the bowel wall affecting its lumen or its elasticity. The tumor may be recognized as more or less of a filling defect, perhaps involving the mucosal pattern only; but more likely, when discovered, it has already invaded the submucous and muscular layers. The **first x-ray sign** may be a localized rigidity of a segment of the intestinal wall. There may be a certain amount of obstruction though not in the early lesions. If the obstruction is of high degree, the filling defect caused by protrusion of the tumor into the bowel lumen will be emphasized or augmented by accumulated nonopaque fecal material proximal to the stenosis. There may be a palpable tumor. If so, under fluoroscopically controlled manual examination, it will be seen to coincide with the filling defect, but the tumor palpated is not always the new-growth itself: A growth too small in itself to be palpable may cause a mass of fecal matter to accumulate above it, or an adherent omentum may add size to the tumor.

The signs just recounted could hardly escape detection in a routine study of the colon, visualized by the ordinary opaque enema, but recognition of the earlier phases of the disease requires a more painstaking and time-consuming effort. In every carcinoma there is a period of lag between the earliest malignant cellular change and the appearance of enough organic alteration to permit of detection by x-ray study. In the average case, by the time the diagnosis is made, symptoms have been present for about a year. Such a diagnosis can hardly be termed "early." Yet, many patients in whom the diagnosis manifestly was not an early one, have survived resection for fifteen or twenty years or more. Failure to discover colonic carcinoma in a very early stage does not necessarily carry with it a bad prognosis as to permanent cure. In the rectum, rectosigmoid and distal colon, early diagnosis of cancer should usually be possible.

The technic used in x-ray study is highly important. The personal equation of the examining radiologist—his experience, versatility, persistence, technical dexterity, and resourcefulness in utilizing the various possible modifications of technic in these studies—has a bearing on his success.

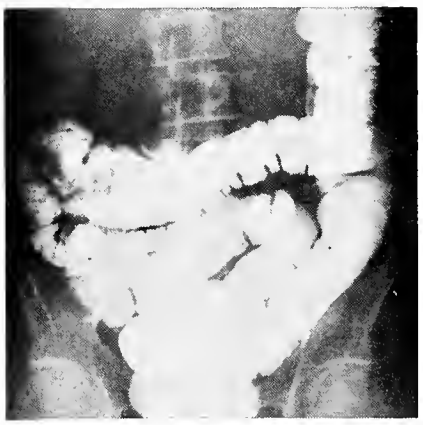
X-ray study of the colon is not standardized, as are many of the procedures of the clinical labora-

tory; every patient presents an individual problem, and it is highly important that the radiologist, like any other medical consultant, should have at his disposal all the knowledge previously gained by the referring physician.

It is necessary to individualize the study. If a lesion in the sigmoid is suspected, because of physical findings, the entire colon should not be filled at first. In order to avoid overlapping shadows from the proximal colon or terminal ileum, the sigmoid and part of the descending colon are first visualized and studied carefully; aimed roentgenographic exposures are made on the fluoroscopic table, with compression or turning of the patient, and the opaque material is then allowed to be discharged. The colon may then be refilled, if desired, and further studies made or it may be injected with air, all the while turning and manipulating the patient to bring into relief every inch of the suspected bowel. If the cecum or ascending colon are under suspicion, special care should be exercised not to overfill the cecum, because some of the material may then enter the terminal ileal loops which may overlap and confuse the cecal shadows. The filling defect of carcinoma of the colon may be imitated by fecal matter, spasm, extrinsic tumors, pressure on ridges or other bony parts, adhesions, diverticulitis, gas and peristaltic movements.

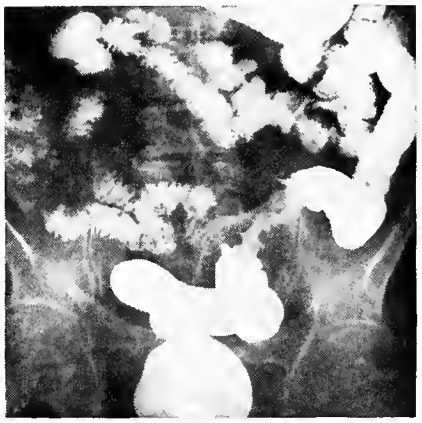
In the average examination of the colon it may be justifiable to conduct the x-ray study in routine fashion, but **if preliminary endoscopy or symptoms indicate the probability of colonic pathology,** it will be best the night before to prepare the colon with cleansing enemas or otherwise eliminate all possible residues. It is highly desirable to have a dry bowel for x-ray study. The injection of the colon should

FIGURE III



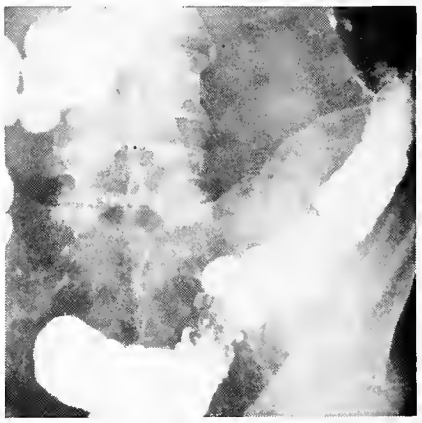
Symptomless carcinoma of the hepatic flexure, discovered by x-ray in the course of a routine physical examination. Surgically removed. Patient survives, after twenty years.

FIGURE IV



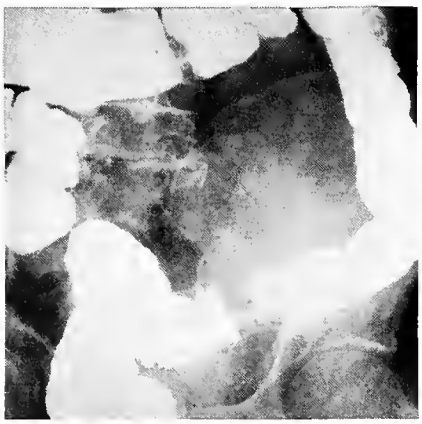
Carcinoma of the sigmoid.

FIGURE Va



Diverticulous inflammatory lesion in the sigmoid. Patient disregarded advice to have semi-annual re-checks.

FIGURE Vb

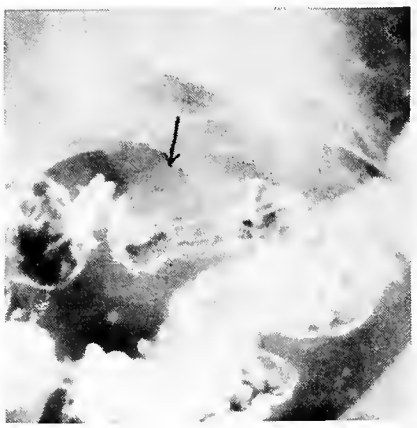


A year and a half later a definite carcinomatous lesion was found.

FIGURE VIa

Slight irregularity in contour of sigmoid.

FIGURE VIb



Compression technic revealed a definite lateral wall carcinoma of the sigmoid.

be watched under the fluoroscopic screen. The examiner, with carefully protected hands or with a wooden, specially shaped palpator, should palpate over the visualized portion of the bowel to test its mobility, and make compression in an effort to discover a lesion otherwise concealed.

Most important, however, after the colon has been visualized and studied, is observation following discharge of the contrast enema. This, plus supplementary air distension of the bowel and making of stereoscopic films, will offer maximum assurance against overlooking small lesions. Studies made after contraction of the colonic lumen (following discharge of the opaque material) are usually more informative than films made while the colon is fully distended. If supplementary air distention is desired, it should be accomplished under screen observation. Great care should be exercised to **avoid overdilating the colon,** not because of any great danger of rupture but because overdilatation provides less information than moderate distention. Also, it is undesirable to force air through the ileocecal valve into the terminal ileum, because this interferes with the interpretation of the colonic shadows.

CANCER OF THE UPPER RESPIRATORY TRACT

Early diagnosis of cancer of the upper respiratory tract (sinuses, larynx, and trachea) is usually accomplished by mirror or endoscopic examination. X-ray studies afford a supplementary method for estimating the extent of invasion of the surrounding tissues.

PRIMARY PULMONARY NEOPLASMS

Pulmonary neoplasms have exhibited a marked increase in recent years. There is a wide and sometimes confusing variation in the x-ray appearance of these lesions, but **most of them are radiographically recognizable,** provided the examiner does not overlook the possibility of encountering them.

It may be necessary to supplement the ordinary x-ray search with **laminagraphic study** or with a bronchographic examination, after instilling an opaque medicament, such as iodized oil, into the bronchi.

The x-ray examination aids in determining the details of the growth of the neoplasm and its effect upon neighboring tissues. Tumors of the main bronchus usually progress by infiltration into the mediastinal lymph nodes, the peripheral lymphatics and, in some cases, the pleura. Bronchial obstruction may become partial or complete at any time, causing obstructive emphysema, atelectasis, and bronchiectasis. If the neoplasm arises from a smaller bronchus, the infiltration is of a more localized type, with early lymph node involvement and more localized atelectatic signs. If the neoplasm originates from a smaller main bronchus in the periphery of the lung, it causes infiltration of the peripheral portion of the lung and may even invade the chest wall or diaphragm. A tumor of parenchymal origin may develop round or lobulated masses which grow by expansion, causing late involvement of the lymph nodes. The stenosing tumors of the main bronchi result in typical massive atelectasis of the involved lung.

The exact site and contour of the obstruction is easily determined by **instillation of lipiodol** into the affected bronchus. It may be possible to depict the actual filling defect or stenosis in the bronchus. **Atelectasis** accompanied by irregular infiltration at the roots of the collapsed lung or by signs of metastatic involvement of other structures indicates a strong probability of cancer. **Paralysis of the diaphragm** due to pressure upon the phrenic nerve by carcinomatous lymph nodes at the lung root may betray a carcinoma. Scalloped shadows along the inner side of the chest wall or a pleural effusion may suggest an intrathoracic malignant growth. Bone metastases in ribs, spine or elsewhere are frequent with bronchiogenic carcinoma.

In atelectasis, failure of the heart to be displaced also suggests the presence of fluid in the pleura. The most frequent cause of the combination of atelectasis plus pleural effusion is a neoplasm of a main bronchus. Sometimes an early malignant lesion without atelectasis may be completely hidden by the mediastinal structures, though not for long. Extension of the disease, causing radiating nodular shadows to spread out from the site of the lesion, will soon disclose its presence. Neoplasms of larger bronchi, as already mentioned, may often cause invasion of the lumen. Such lesions may be recognized by the use of iodized oil.

Carcinoma of a smaller bronchus resembles an unresolved pneumonia. The differentiation may be very difficult, but observation of the progress of the case soon clears up the diagnosis.

Except in advanced stages, **the usual primary malignant lung tumor is small** and may not be demonstrable except by the use of iodized oil. The lesion is recognized by the complications and associated pathology resulting from the bronchial obstruction and lymphatic spread. A small localized malignant tumor in the periphery of one of the lobes presents a fairly well localized shadow of homogeneous density. This shadow either in antero-posterior or lateral projection will usually present a somewhat triangular shape due to the spread of the lesion distally from its point of origin.

Differential diagnosis is often difficult. Inflammatory lesions must be excluded; sometimes they are coexistent. Serial study of the suspected area may aid. If bone absorption occurs in a rib, or the invasive type of the lesion becomes manifest in any other way, the diagnosis is facilitated.

METASTATIC CANCER OF THE LUNG

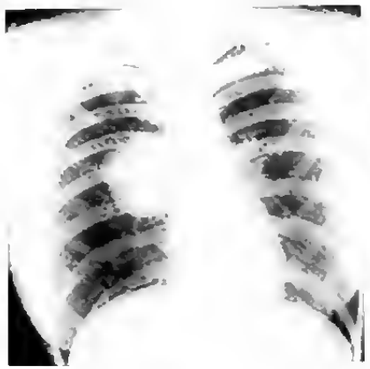
Discussion of metastatic cancer involvement may seem out of place in an article devoted to early cancer diagnosis. It is included, however, because metastatic cancer in the lungs is not an infrequent incidental finding, and differential diagnosis between primary and secondary invasion then becomes important.

Metastatic neoplasms of the lung are readily disclosed on roentgen examination, though often overlooked on physical investigation. There are two general type of metastatic involvement: the nodular and the diffuse.

Metastatic nodules are nearly always seen as multiple, rounded masses of varying size, more numerous in the lower than in the upper chest. When the metastatic tumor is **solitary,** it may assume large size; when metastases are **multiple** but few in number, they may vary greatly in size; when **numerous,** the lesions are often more or less uniform and of relatively small size. Metastatic nodules are, in general, of rounded form, but lobulated borders are sometimes presented by the metastatic extensions of hypernephroma or carcinoma of renal origin.

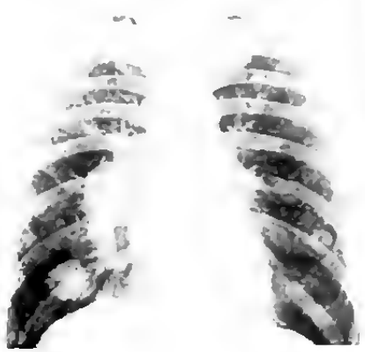
Differentiation between metastatic carcinoma and metastatic sarcoma may not be possible from simple x-ray study of the chest. Carcinomatous metastases sometimes show irregularity in density because the lesions are not absolutely homogeneous, whereas the metastatic nodules of sarcoma are homogeneous and uniform in structure, and present a sharply bordered, rounded shadow of perfectly uniform density. Pulmonary malignant metastases may simulate cysts or even primary neoplasms, but they grow rapidly, whereas cystic changes do not undergo rapid variation.

FIGURE VII



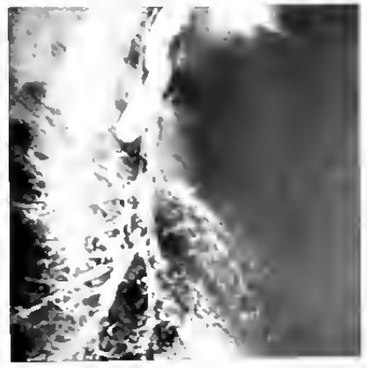
Primary sarcoma of the lung.

FIGURE IXb



Shows pulmonary metastasis

FIGURE VIII



Primary carcinoma of the lung, stenosing right main bronchus, as demonstrated with lipiodol bronchography

FIGURE X

Papillary tumor of the bladder

FIGURE IXa

Osteolytic sarcoma of the first metatarsal bone already metastasizing

FIGURE XI

Giant-cell tumor of the radius

The infiltrating or diffuse type of metastatic pulmonary involvement is shown as streaks or fine nodules, radiating throughout the pulmonary fields. The most common example of lymphangitic spread is seen in gastric carcinoma, but may also be seen with mammary or pancreatic neoplasms. The spread is usually by way of the local lymphatic channels communicating with those of the lung, the lymph vessels being gradually replaced by tumor tissue. The progression of such lesions is strikingly rapid. The denser shadows occur in the hilum of the lung, being due not only to the convergence of lymphatic channels but also to the enlargement of the peribronchial and mediastinal lymph nodes.

The most common malignant lesions in the pleura are metastatic, having migrated to this site from cancer of the breast, stomach, kidneys or other organs, but most commonly from the lung. They usually produce a pleural effusion, though sometimes the malignant nodules themselves may be seen as scalloped shadows in the periphery of the lung fields, or in the costophrenic sinuses. This is noted especially after withdrawal of the pleural effusion and placing the patient in an erect or lateral or partly inverted position as may be best calculated to throw the malignant lesion into relief. Primary pleural neoplasms are rare.

CANCER OF THE KIDNEY

Renal cancer includes papillary adenocarcinoma (most of the so-called hypernephromas), alveolar carcinoma, true hypernephroma originating from adrenal rests, and Wilms' tumors.

Carefully-made survey roentgenograms of the renal region will often show a variation from the normal smooth-bordered, regular renal contour, so that the presence of a tumor may be recognized, but **intravenous or retrograde urography is an important diagnostic method** for determining the nature of the renal tumor. The enlargement may be confined to one pole, as shown by urography, or there may be diffuse large masses. Displacement of the renal pelvis downward may be caused by upper pole tumors (hypernephromas, as a rule, arising in the upper pole) or by adrenal neoplasms. If there is no invasion of the pelvis itself, the presence of the tumor may be betrayed simply by the displacement and distortion; the calices may be reduced in size, displaced, and apparently narrowed, due to rotation, but they show cupping. If the lesion is an adrenal tumor, and remains extra-renal, the displacement and rotation may be the only signs of the tumor. **Hypernephroma,** however, usually shows more or less renal invasion. These tumors tend to develop areas of calcification of an irregular pattern; sometimes they develop well defined, large masses.

Intra-renal tumors or intra-renal extensions of tumors cause elongation and characteristic distortion of the calices in the vicinity of the tumor. The calices are lengthened and narrowed and their cups distorted, the infundibula remaining only as streaks. When the pelvis is invaded by a tumor mass or a large blood clot, a pelvic filling defect results, as shown in urograms. Finally, if the tumor involves the ureteropelvic junction, obstruction occurs with the development of hydronephrosis.

To be differentiated are such benign renal tumors as adenomas, solitary cysts, fibromas, lipomas, angiomas and multiple cysts. These benign tumors are rare.

Ureteral neoplasms are also rare but may be recognized by the filling defect in the ureter. The combination of intravenous and retrograde urograms may give most exact information regarding ureteral neoplasms.

CANCER OF THE BLADDER

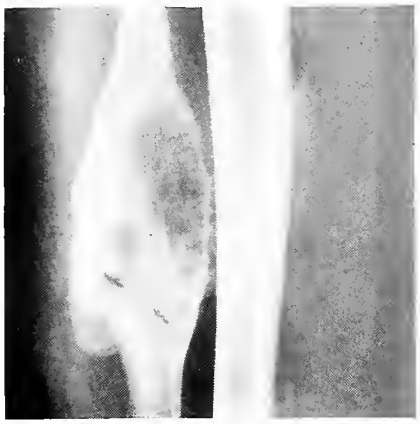
Cystograms are most important in the study of bladder tumors; they often suffice to make a diagnosis in cases of hemorrhage where cystoscopy seems unwise. The neoplasm is recognized by an irregular filling defect in the otherwise diffuse, opaque shadow of the filled bladder, or by a filling defect thrown into profile causing a recognizable irregularity in the bladder contour. In large lesions the filling defect in the cystogram is easily recognized. Differentiation must be made between an intravesical neoplasm and a tumor of an adjacent organ growing into the bladder.

With very small or flat tumors, causing small defects, the lesion may easily be overlooked or overshadowed by the density of the contrast medium employed for the cystography. Some radiologists prefer to make a supplementary air cystogram immediately after the opaque material has been evacuated, after which stereoscopic films of the bladder are highly informative.

CANCER OF THE BONE

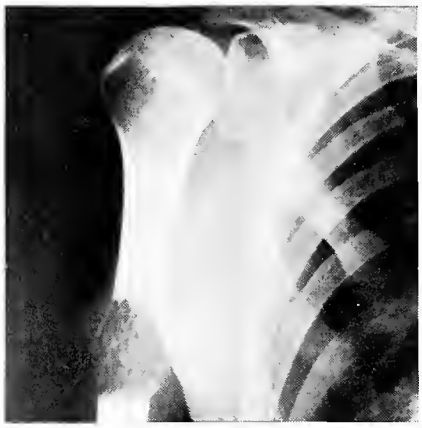
In differentiating benign and malignant bone tumors it may be said that when the contour of the shadow cast by an osseous tumor is unbroken, with few exceptions the lesion is benign. **A sudden break in the contour of the bone speaks for malignancy.** When invasion of surrounding tissue has taken place, lack of definite demarcation of the invading portion of the tumor emphatically suggests a malignant lesion. On the other hand, if the invading portion continues its definite demarcation, this encapsulation is an indication of a benign lesion. With few exceptions, defects in flat bones, even large flat bones, are benign when characterized by smooth, definitely outlined margins, whereas malignant

FIGURE XII



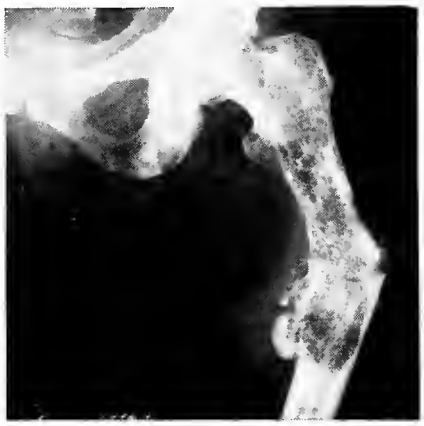
Ewing's sarcoma of the fibula. (Lower end of illustration shows proximal portion of fibula.)

FIGURE XIII



Metastatic hypernephroma in the humerus.

FIGURE XIV



Metastatic mammary carcinoma in the femur and ischiatic bone.

lesions are usually marked by irregular or indefinite, dentate borders.

Cartilage is practically invisible on roentgenograms; **fibrous tissue** casts a certain amount of shadow; **bone** causes a definite shadow. Many tumors consist of a combination of these tissues, and their nature may be estimated according to the degree of translucency to the x-rays. There are certain exceptions to these rules, however, such as giant-cell tumors, Ewing's tumors, and myeloma.

Giant-cell tumor appears as a single, central lesion near the epiphysis of a long bone. It tends to extend, but sometimes shows growth along the path of least resistance, the medullary canal. In these lesions, cortical bone bulges but rarely breaks.

Myeloma is a highly malignant lesion in which the shaft of the ribs and long bones may be distended without a break in contour and without invasion of neighboring tissues. Myeloma usually appears as multiple, round or oval defects, punched-out in appearance, seen in ribs, sternum, skull, thoracic and lumbar spine and pelvic bones.

Ewing's bone sarcoma, characterized by diffuse infiltration with widening and increased density of the cortex and an elliptical, symmetrical expansion of the shaft, usually occurs in the middle of a long bone. New-bone formation predominates, usually giving rise to parallel (onion skin) laminae but sometimes to radiating spicules; invasion of the soft tissues results in a less definite encapsulated shadow than that cast by most benign tumors.

Chronic sclerosing osteitis, nonsuppurating osteomyelitis of Garré, traumatic and other types of osteomyelitis, traumatic osteoma, subperiosteal hematoma, osteitis deformans, osteitis fibrosa cystica, and exostoses resemble cancer of the bone roentgenographically, and require differentiation.

Carcinoma in bone is usually metastatic and generally multiple, involving any one or all of the bones. It is not often found in the extremities below the knees or the elbows. **Two general types may be observed:** Osteolytic forms, characterized by irregular destruction of bone substance, with no periosteal reaction and no change in contour unless fracture or compression occurs; and the osteoplastic forms, usually secondary to prostatic or mammary carcinoma and shown by extensive production of dense bone, with coarse mottling due to intermingled areas of rarefaction and condensation, and sometimes with enlargement of the bone suggestive of osteitis deformans. Metastases from hypernephroma have a predilection for bone. Testicular and bladder disease rarely metastasize to bone. Ovarian malignancies rarely cause skeletal disease. The same may be said of the digestive tube. About 15 per cent of malignant disease of the lung metastasizes to bone. Osteogenic sarcoma may present multicentric growths. All of these metastatic lesions may lead to pathologic fractures.

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. 10

THE LARYNGOSCOPE, BRONCHOSCOPE, AND ESOPHAGOSCOPE AS AIDS IN THE EARLY DIAGNOSIS OF CANCER

The keen powers of observation that characterized the physicians of past generations are almost legendary. One glance often established a diagnosis later substantiated by hours of careful physical examination and days of observation. The physician of today has not lost the art of inspection which was so stressed by his teachers; he has increased its scope a hundredfold by electrically lighting the many body cavities and searching their every fold and corner. Thus, he is able to visualize areas never before seen in the living patient. He not only obtains information for visual interpretation, but also collects material for laboratory study which infinitely increases diagnostic acumen and may be of lifesaving importance.

LARYNGOSCOPY

The larynx was the first of the lower air passages, not readily visible to the naked eye, to be satisfactorily inspected. In 1856, a singing teacher, wishing to examine the vocal cords of his students, devised the laryngeal mirror. By means of this simple device he was able to study the normal action of the vocal cords. Only later was his discovery used for the diagnosis of laryngeal disease.

Diseases of the larynx are characterized by symptoms of hoarseness or dyspnea. Early cancer of the larynx is rarely silent; the patient, his family, and his physician are immediately aware of a change in voice, because the great majority of early laryngeal cancers affect the phonating edges of the vocal cords (Figure I). But hoarseness is a symptom so frequently associated with the common cold (appearing and disappearing many times during the life of the average individual) that the more serious significance of this symptom may be overlooked. This is especially true when it simply annoys the patient and is not associated with any degree of pain or discomfort. Early cancer of the larynx is *not* generally associated with pain, except in those rare instances in which it originates on one arytenoid or on the posterior surface of the epiglottis.

Inspection of the larynx is the first step necessary when hoarseness develops, especially if the hoarseness is *persistent, pronounced, and progressive.* The laryngeal mirror permits a preliminary study, but often a gagging patient or an overhanging epiglottis does not permit inspection of the anterior tips of the vocal cords, the area in which early cancer of the larynx is most frequently found (Figure IV). For inspection of this all-important area the laryngoscope was developed.

The laryngoscope consists of an electrically lighted tube about six and one-half inches long which, when introduced through the mouth, may be used to retract the epiglottis and thus expose the vocal cords. It may be introduced under local anesthesia; as it reaches the cords it gives a full view of the anterior tips of the cords. It also permits inspection of the laryngeal ventricles and subglottic space, areas hidden from the mirror view by the overhanging false and true cords (Figure VI). Of utmost importance is the fact that the laryngoscope enables the operator to remove tissue from suspicious areas or from actual ulcerative or proliferative processes for biopsy purposes (Figure V).

Direct laryngoscopy is a relatively simple procedure in proportion to the amount of information which may be obtained by it. Early cancer of the larynx is more amenable to cure than most cancers; direct inspection of the larynx, through the laryngoscope, can aid in detecting the lesion while still curable.

BRONCHOSCOPY

The bronchoscope, also simply an electrically lighted speculum, aids in the detection of early cancer of the lung. Bronchogenic carcinoma (so-called because all lung cancer has its origin in the bronchi rather than in the alveoli) is no longer a

medical rarity. It ranks second in cancer incidence in males, exceeded only by gastric carcinoma in frequency. Its symptoms and clinical course are extremely variable; consequently, bronchogenic carcinoma must be considered as a possible diagnosis in any pulmonary disease. Cough, tightness or constriction of the chest, chest pain, asthmatoid wheezing, and occasional hemoptysis are some of the

FIGURE I

FIGURE II

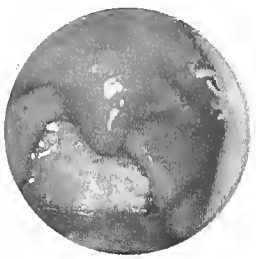


FIGURE I Early carcinoma of phonating edge of right vocal cord. Cord removed surgically; patient living and well.

FIGURE II Ulcerative carcinoma of pharynx and hypopharynx extending downward to involve cervical esophagus.

symptoms of *early* carcinoma of the lung. These symptoms or the actual demonstration of a bronchial obstruction require first a thorough x-ray study of the chest, and next a bronchoscopic examination. Not infrequently, the first evidence of pulmonary cancer is an acute pneumonic process which is readily mistaken for pneumonia, virus pneumonia or, later, for unresolved pneumonia. The role which the bronchoscope plays is that of assisting in the differential diagnosis of these lesions.

Visualization of the major bronchi through the bronchoscope is a well recognized procedure, devised originally for the removal of foreign bodies that had been aspirated. It is not so well understood that foreign bodies can be removed from almost any portion of the lung with the assistance of the biplane fluoroscope, the bronchoscopic forceps being directed under the fluoroscope. Procedures similar to those used for the removal of foreign bodies may likewise be used for the recognition and localization of tumors, and for the removal of tissue for biopsy purposes. Various improvements in bronchoscopic technic, as well as in laboratory analysis, have raised to more than 75% the proportion of cases in which a positive histologic diagnosis of bronchogenic carcinoma can be made (Figure III).

Bronchogenic carcinoma, as is so often the case in carcinoma anywhere in the body, may easily be overlooked because of complications which in themselves are sufficiently important to be mistaken for primary conditions. A lung abscess or extensive bronchiectasis falls into this category so frequently that it becomes imperative that every patient with either of these conditions should have at least a diagnostic bronchoscopy, to establish the presence of a carcinoma or to rule it out. The alleviation of symptoms through the use of penicillin, even the apparent improvement on x-ray that follows penicillin therapy in pulmonary suppuration, should not be considered as justification for delaying or eliminating the bronchoscopic examination. Similarly, a delay of six weeks to two months, while awaiting the results of a guinea pig inoculation of the sputum or the gastric washings of a patient suspected of having tuberculosis, too often results in making inoperable a carcinoma which might have been resected.

Bronchoscopy, even in tuberculous patients, is a procedure that may be done without trauma, under local anesthesia. The major bronchi and their primary subdivisions may be inspected through the open tube itself. The orifices of the upper lobes may be inspected with retrograde telescopes. The bronchoscopic forceps may be guided to a tumor under the fluoroscope or directed into upper lobe orifices after an artificially induced pneumothorax. In most instances, the bronchoscopic examination is brief, and there seems little reason for delaying its use as a diagnostic procedure. Not only can tissue be removed for histologic study, but various criteria can be ascertained which will aid in determining the operability or inoperability of the tumor.

At this point it may be well to state that, while in some instances a negative bronchoscopic examination is important in ruling out bronchogenic carcinoma, in other instances further diagnostic

FIGURE III

FIGURE IV

FIGURE III Bronchogenic carcinoma of left upper lobe bronchus. Tumor covered by purulent secretion; biopsy showed a squamous cell carcinoma. Left lung resected; patient living and well.

FIGURE IV Carcinoma of anterior commissure of larynx, involving anterior tips of both vocal cords. Laryngectomy performed to remove the tumor.

studies may be indicated if a tumor is still suspected and not found. Exploratory thoracotomy may be performed as safely as exploratory laparotomy when additional information, not obtained bronchoscopically, is needed. In a disease as insidious and masked as bronchogenic carcinoma frequently is, every diagnostic means must be employed to detect its pres-

ence. The chest x-ray gives only a *presumptive* diagnosis in most cases. A bronchoscopic examination usually provides the *actual* diagnosis, by furnishing material for histologic examination.

ESOPHAGOSCOPY

Until recently, the hopeless prognosis formerly associated with the diagnosis of carcinoma of the esophagus made early diagnosis of this lesion largely a matter of academic interest. However, the advances in thoracic surgery during the past ten years

FIGURE V

FIGURE VI

FIGURE V Ulcerative carcinoma of right vocal cord.

FIGURE VI Subglottic carcinoma, hidden under right vocal cord, visible only after lateral retraction of true cord by laryngoscope.

have made possible the successful resection of carcinoma of the esophagus. This has resulted in the cure of a sufficient number of patients to make the early diagnosis of carcinoma of the esophagus imperative. The initial symptoms and, consequently, the indications for esophagoscopy, in carcinoma of the esophagus, are due to impairment of the swallowing function. This may be in the nature of a slight dysphagia, a feeling of a lump in the throat, or increasing difficulty in swallowing solids. Occasionally the symptoms are so insidious that the patient slowly alters his eating habits over a period of weeks or months, but the reverse may also be true. Complete, sudden inability to swallow is the initial symptom, as a bolus of meat lodges in a malignant obstruction.

As noted in regard to bronchoscopy, if esophageal symptoms present themselves, x-ray studies are indicated before any esophagoscopic examination is made. These studies should consist of flat plates of the neck and chest and fluoroscopic studies of the esophagus with barium. In most instances, the irregularities characteristic of a neoplasm will be apparent from the latter examination. However, in no case should the diagnosis be considered as established without an esophagoscopic examination of the lesion and histologic confirmation with tissue removed through the esophagoscope.

The esophagoscopic examination becomes of even greater importance when symptoms suggest carcinoma but x-ray studies are negative. Early lesions will not produce filling defects, consequently, visual examination should supplement fluoroscopy in such instances. This is especially true of lesions in the cervical esophagus through which the barium column is propelled with such speed that defects are not readily outlined.

The esophagoscope, like the laryngoscope and the bronchoscope, is an electrically lighted tube twenty-one inches in length and, for diagnostic purposes, less than one-half inch in diameter. It may be introduced through the mouth under local anesthesia. Its beveled tip lifts the larynx forward to slide into the esophagus. In the hands of those familiar with its use, the examination does not entail any appreciable risk. The interior of the lumen of the esophagus may be thoroughly inspected, from the hypopharynx to its entrance into the stomach. Ulceration, induration or actual tumor tissue obstruction of the esophagus may be noted and tissue may be removed for histologic examination with proper biopsy forceps (Figure II).

SUMMARY

In summary, it may be stated that the laryngoscope, the bronchoscope, and the esophagoscope permit routine examination of body cavities otherwise inaccessible. The safe visual inspection which these instruments afford helps to detect cancer of the larynx, the bronchi, and the esophagus at a stage during which its elimination, either surgically or otherwise, will be possible in a great number of patients. The principal symptom of early laryngeal cancer for which the use of the laryngoscope is indicated is *hoarseness*. A persistent cough, recurring or unresolved pneumonia, tightness, pain or constriction of the chest, occasional hemoptysis or the actual demonstration of a bronchial obstruction are symptoms and signs of bronchogenic carcinoma. They may be temporarily alleviated through the use of penicillin, but actual visualization through the bronchoscope must be considered one of the routine diagnostic steps in diseases of the chest. Negative x-ray findings in the presence of these symptoms do not necessarily rule out the possibility of a bronchial tumor. Dysphagia, changes in eating habits, and the sensation of a lump in the throat are some of the characteristic symptoms of early esophageal carcinoma. Thorough x-ray studies followed by esophagoscopic examination are essential to overcome the formerly hopeless prognosis of esophageal carcinoma. As Clerf has stated, "We, as clinicians, may not be able to find the cure for cancer, but let us at least detect its presence at a time when it may still be eradicated!"

THE ROLE OF PROCTOSCOPY IN THE EARLY DIAGNOSIS OF CANCER OF THE RECTUM AND SIGMOID COLON

The terminal bowel—the rectum and sigmoid colon—lends itself well to direct endoscopic visualization. Proctosigmoidoscopy represents an ingenious and extremely helpful procedure for confirming the diagnosis in palpable rectal cancer, for discovering impalpable cancerous growths in the lower colon beyond the reach of the examining finger in the rectum, and for noting precancerous lesions, of which polyps are notable examples. Scientific medical practice could no longer do without the method.

Buie says that three-fourths of all colonic cancers occur in that part of the bowel which can be directly visualized through the proctosigmoidoscope. It is therefore obvious that every patient whose history suggests the slightest possibility of rectal or colonic disease should have the benefit of a competent endoscopic examination. Even though cancer is not found, a remediable precancerous condition may be discovered, while an entirely negative result would be comforting both to patient and physician.

The insertion of the proctosigmoidoscope must always be preceded by thorough inspection and palpation of the anal and perianal tissues, followed by a careful digital exploration of the anal canal and rectum. The insertion of the well lubricated finger serves to lubricate the anal canal and to warn the examiner of the presence of any mass or lesion which might interfere with the safe passage of the endoscope.

The "inverted" position, afforded by a suitable tilt-table or by the knee-shoulder position, greatly facilitates proctoscopy. The instrument is passed gently into the anal canal, the long axis pointing toward the umbilicus. As the tip of the instrument passes proximal to the anal sphincters, its further progress is momentarily halted while the examiner removes and lays aside the obturator or mandarin. Any further passage of the instrument must be made under direct visualization—*never blindly*! As the instrument lies in the long axis of the anal canal (position 1, Figure I), the examiner can view the anterior wall of the rectal ampulla. Accordingly, he must alter the course of the instrument if he is to avoid trauma to the anterior rectal wall, this being the most common site of "enema tip injuries." The proximal end of the instrument is then depressed (from position 1 to position 2, Figure I), bringing it into the long axis of the rectum, which is approximately at a right angle to the long axis of the anal canal. It can then be advanced slowly, *under direct vision*, to the left or to the right, around and past the rectal valves, beneath one fold or above another, until the distal end lies beneath or distal to the sacral promontory. At this point it is necessary to warn the patient of a cramp in the upper abdomen, caused by "levering" the distal end of the instrument anteriorly so as to clear the promontory, a maneuver which entails some traction on the mesosigmoid. The instrument, having cleared the promontory of the sacrum, can then be passed into the distal segment of the sigmoid colon (position 3, Figure I below).

FIGURE I

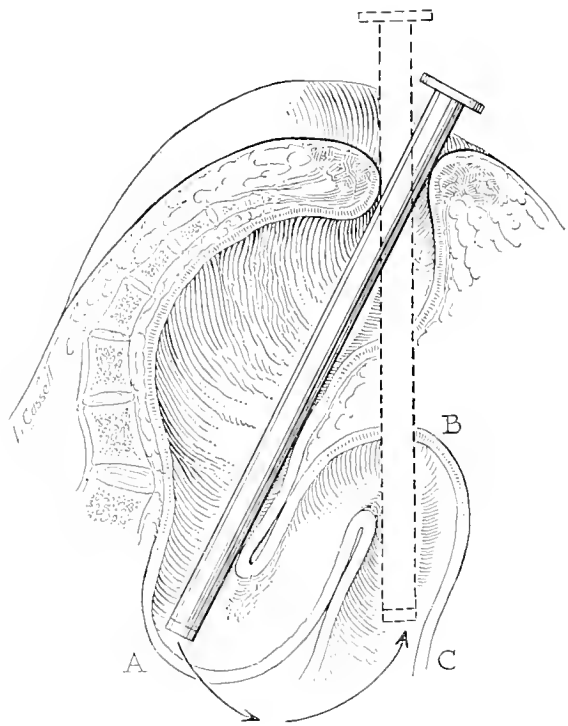
[illegible]

Not uncommonly, the experienced endoscopist finds that the tip of the fully inserted endoscope lies in a blind pouch (Figure II, A). By slowly withdrawing the instrument and at the same time carefully levering the distal end anteriorly, he may succeed in advancing the tip to point B, Figure II. The proctoscopist should then be able to reach point C, Figure II. By means of this maneuver he has been able to examine the more proximal segment of bowel from A to B and the still more proximal segment from B to C (Figure II)—perhaps an additional six or eight centimeters of gut—and yet the proctoscope was presumably "fully inserted."

when advanced to point A. This refinement in proctosigmoidoscopic technic pays great dividends in the study of sigmoidal lesions. The midsigmoid is a notorious danger zone, harboring difficulty for both the proctologist and the roentgenologist.

If a lesion is within reach of the examining finger, such pertinent features as fixation, induration, infiltration, etc., can be more readily determined. Should the growth lie beyond reach by the finger,

FIGURE II



Diagrammatic scheme of proctoscopic maneuvers.

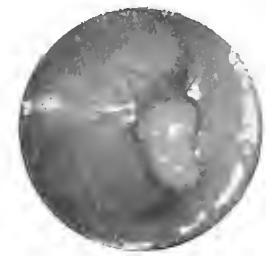
fixation can be estimated by the "feel" of the instrument.

The passage of the endoscope may have been halted, of course, at any point by the presence of an obstructing tumor mass. Obstruction may be sufficient to preclude passage of the ordinary size instrument (5/8 in.), but may allow passage of an instrument of lesser caliber, thus permitting the examiner to determine the proximal extent (upper border) of the lesion.

Carcinoma of the gut may present itself as a sessile, polypoid mass extending into the lumen, or it may be an annular, ulcerating, crateriform lesion causing obstruction by means of constriction.

The examiner should determine as accurately as possible the distance between the lower border of the lesion and the anus, because the amount of normal bowel below the growth is an important factor in the determination of the type of surgical procedure to be used.

FIGURE III

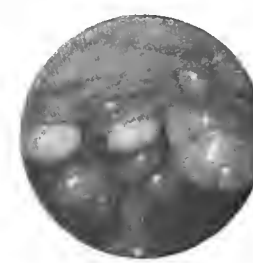


View of a small, sessile polyp, lying on the edge of a rectal valve.

Before withdrawing the instrument, the examiner should remove a piece of tissue from the border of the lesion for microscopic study. Such tissue usually comes away easily in cancer, whereas it separates with difficulty when the lesion is inflammatory (i.e., amebic ulcer, diverticulitis, etc.). The microscopic study offers some help in the grading of malignant tumors and serves to avoid the occasional pitfall offered by amebic granuloma, or by an endometrial lesion of the gut in the female during the childbearing period of her life.

Most roentgenologists agree that roentgenologic study of this part of the gut is difficult at best, whereas the bowel proximal to the point of access by proctoscopy is best studied by means of x-ray. Hence the two procedures should not be pitted

FIGURE IV



Multiple, small, sessile polyps with normal mucosa amongst them.

against each other, but be used as complementary methods in conjunction to facilitate, along with proper stool tests, a thorough study of the entire colon.

CASE REPORTS

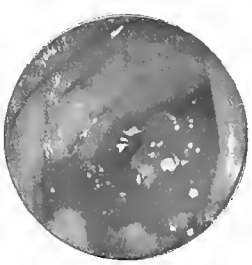
I. H.R.G., a 46 year old white male, complained of pain and bleeding at stool for several weeks, and of a feeling of "unfinished business" after stool for six months. Preliminary examination revealed an acute posterior anal fissure.

On proctoscopic examination there was found a large, crateriform, ulcerating lesion involving the anterior, left and posterior walls of the upper one half of the rectum. Lower border of the lesion was at 9 cm. and the upper border at 12 cm. Obstruction grade II. Fixation grade II. Tissue removed for microscopic study. *(Lesion within easy reach of finger.)*

Diagnosis: Carcinoma, rectum.

II. E.M.S., a 55 year old white male, complained of rectal bleeding at stool, and of gradually increasing difficulty at stool for

FIGURE V



Small, polypoid carcinoma lying in the distal portion of the sigmoid colon.

six months. In addition there were frequent loose stools.

He had been treated for three months for amebiasis by his physician, during which time no digital exploration of the rectum was made. The patient had lost twenty pounds in six months.

On proctoscopic examination there was found a large, annular, ulcerating growth of the rectum, beginning 8 cm. above the anus and involving the upper one third of the rectum. Obstruction grade III. Fixation grade III. Tissue removed for microscopic study. *(Lesion within easy reach of finger.)*

Diagnosis: Carcinoma, rectum.

III. C.D.B., a 78 year old white male, complained of rectal bleeding and diarrhea for five months.

On digital and proctoscopic examination there was found an ulcerating carcinoma involving the middle one third of the rectum. The lesion was almost annular except for a narrow strip of mucous membrane on the right anterior portion. The upper limit of the lesion was at 13 cm. On the anterior wall of the rectosigmoid, at 13 cm., was a

FIGURE VI

Large carcinoma of the rectum, lying within easy reach of the examining finger.

small ulcerating lesion 2 x 2 cm. in size. Tissue removed for microscopic study.

Diagnosis: 1) Carcinoma, rectum.
2) Carcinoma, rectosigmoid.

IV. W.W.R., a 40 year old white male, complained of steadily increasing difficulty at stool, with some bleeding for four months. On digital and proctoscopic examination there was found an ulcerating carcinoma involving the posterior and both lateral walls of the middle one third of the rectum, from 6 to 10 cm. above the anus. Obstruction grade II. Tissue removed for microscopic study.

Diagnosis: Carcinoma, rectum.

V. T.M., a 66 year old farmer, complained of severe itching for twenty years! *No other complaint.*

On proctoscopic examination there was found, beginning 9 cm. above the anus, a polypoid growth 3 x 2 x 1 cm. in size involving the anterior wall of the upper one third of the rectum. No obstruction. No fixation. Tissue removed for microscopic study.

Diagnosis: Carcinoma, rectum.

●

THE CANCER BULLETIN No. 11 will present a comprehensive discussion on "The Early Diagnosis of Gastric Cancer by the Use of the Gastroscope."

BULLETIN No. 12 will contain special articles on "The Early Diagnosis of Cancer in the Genitourinary Tract" and "Applied Biopsy in the Early Recognition of Cancer." These will complete Volume I of THE BULLETINS.

A supplementary number, with a treatise on "Heredity and Cancer," will follow. The future of THE BULLETIN will also be discussed in the supplement.

Color plates furnished through the courtesy of What's New, September 1946

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. I NO. II

THE EARLY DIAGNOSIS OF GASTRIC CANCER BY THE USE OF THE GASTROSCOPE

Gastroscopy is an endoscopic method which permits the direct visualization of the mucous membrane of the stomach. The procedure, as performed by a trained specialist, is safe and relatively simple. The examination is carried out in the clinic or office, requires only several minutes, and can be repeated at frequent intervals when necessary.

The chief limitation of gastroscopy is the inability to visualize all parts of the stomach. The most important of these "blind" areas is the lesser curvature of the antrum, a common location for carcinoma. There are few contraindications to the method: Intrinsic disease of the esophagus (such as varices, diverticula and stricture), carcinoma of the esophagus or cardia, aortic aneurysm, angina pectoris, severe kyphoscoliosis, and psychosis.

GASTROSCOPY AS A COMPLEMENTARY METHOD TO THE X-RAY

The standard method for early diagnosis of gastric carcinoma is the roentgen examination of the stomach. Its importance has been emphasized in a previous issue of the BULLETIN. However, the roentgen findings are not always conclusive. Such lesions as superficial ulceration, early infiltration, or small tumors may be recognized best by gastroscopic examination. Conversely, the roentgen study occasionally demonstrates a lesion which cannot be seen gastroscopically. The point to be emphasized is that the two methods supplement each other; when used co-operatively, they make possible the diagnosis of almost all cancers of the stomach.

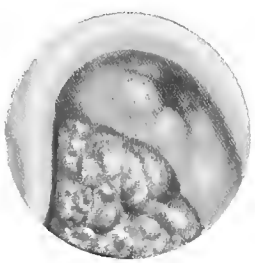
Gastroscopy possesses a particular advantage in that the picture, because of the presence of circulating blood, is sharp and colorful. There are striking contrasts between the brilliant, glistening, orange-red appearance of the normal mucosa and the dull-gray, brown, or red appearance of a pathologic process. These contrasts occasionally make the gastroscopic aspect of a lesion more informative even than the examination of the gross specimen. Cases 1 and 2 demonstrate the value of gastroscopy as a supplementary diagnostic procedure to the x-ray.

Case 1: A man aged 42 years experienced gnawing pain in the epigastrium, one hour after meals, for six months. Food and alkali afforded partial relief. Vomiting, loss of appetite, and weakness developed subsequently. Gastric analysis after stimulation with histamine, revealed the presence of free hydrochloric acid. The stools were strongly positive for occult blood. Roentgen examination revealed a stenosing lesion at the pyloric end of the stomach and duodenal bulb. The impression was that of a peptic ulcer, although carcinoma could not be excluded with certainty. The examination was considered unsatisfactory and its repetition was advised after gastric aspiration. Gastroscopy demonstrated a huge carcinomatous ulcer on the lesser curvature, above the angulus. The tumor had a limiting wall toward the antrum and anterior wall of the stomach, but the ulcer blended with the neighboring mucosa toward the lesser curvature. This infiltration extended to within 2-3 cm. of the cardia. The surrounding mucosa was atrophic. A second roentgen examination, after gastroscopy, likewise demonstrated a diffuse carcinoma of the lesser curvature, extending almost to the esophageal orifice, and containing a flat ulcer. Operation revealed a large carcinoma on the lesser curvature extending upward to the cardia. The microscopic diagnoses were carcinoma simplex and extensive atrophic gastritis.

Comment: The first roentgen examination was unsatisfactory and thus did not permit a conclusive diagnosis of carcinoma as was possible at the initial gastroscopy. A second roentgen study confirmed the gastroscopic findings.

Case 2: A man aged 57 years had experienced gnawing pain in the epigastrium, two hours after meals, for one year. This symptom was accompanied by pyrosis and impairment of the appetite. Food and alkali afforded relief. In the two months prior to examination, the epigastric distress was almost completely relieved by antacid therapy. However, the patient lost fifteen pounds in weight during this period. There was slight tenderness in the epigastrium on physical examination. Free hydrochloric acid was present in the gastric content after stimulation with histamine. Roentgen examination revealed

Figure 1



Polypoid, nodular carcinoma (type I) on the greater curvature of the antrum. Severe atrophic gastritis.

a constant, rounded defect on the lesser curvature, just proximal to the pyloric canal. An ulcer crater was suspected. A second examination demonstrated a small lesion on the lesser curvature of the antrum. The lesion was thought to represent either a small neoplasm with a central crater, or a benign ulcer with considerable inflammation about it. One month later a sharply circumscribed ulcer crater, 6 cm. in diameter, was seen proximal to the pylorus. The crater was surrounded by a collarlike stiffness of the gastric wall. The roentgen impression was that of a prepyloric ulcer, probably benign, but malignancy could not be excluded.

Three gastroscopies were performed. At the first examination, a distorted pylorus, overlapped by two protruding nodes, was visualized, and suggested the presence of a malignancy. Operation, therefore, was recommended. Severe hypertrophic gastritis of the lower portion of the body of the stomach also was noted. Essentially similar findings were observed in the second and third examinations. The mucosa of the greater curvature of the antrum, however, appeared gray, thin, and atrophic. The final gastroscopic examination revealed a distinctly pathological-appearing pylorus. Its ring was stiff, irregular in shape, and definitely infiltrated. One large node protruded from the posterior wall, and another between the anterior wall and the greater curvature. Between this latter node and the pyloric ring, an irregular, small, dirty-gray ulceration was seen. The mucosa of the greater curvature of the antrum was smooth, thin, and grayish. The gastroscopic diagnosis was ulcerative and infiltrative carcinoma of the pylorus with atrophic gastritis. At operation, a small lesion was palpated in the pyloric region which was thought to be a benign ulcer. The lesion appeared benign on gross examination. Microscopically, however, a very small carcinoma, measuring 8 mm. wide and 0.5 mm. deep, was seen. The final diagnoses were: (1) carcinoma, partly simplex and partly adenomatous, of minimal size, and (2) extensive atrophic gastritis.

Comment: In addition to the diagnostic appearance of the lesion gastroscopically, still another factor contributed to the correct gastroscopic diagnosis in this case. It is well known that benign ulcer at the pylorus rarely, if ever, is observed at gastroscopy, because scar formation, or adhesions, displace the pylorus upward, out of the gastroscopic visual field. Experience has indicated, therefore, that if a pyloric ulcer can be seen gastroscopically, it is almost always carcinomatous. This rule was applied to the present case and again found to be correct.

This case also illustrates the value of roentgenologic and gastroscopic examinations in patients with only mild digestive symptoms and loss of weight. At the time of the examination, the patient had practically no distress, but had lost 15 pounds in weight.

GASTROSCOPY IN CHRONIC ATROPHIC GASTRITIS

It is a widely accepted theory that gastric cancer does not develop in a completely normal gastric mucosa. Many authorities believe, for example, that extensive atrophy of the gastric mucosa may lead to the formation of benign gastric polyps which later degenerate into malignant tumors. It has been suggested, therefore, that the early diagnosis of gastric cancer will be facilitated if (a) gastroscopy is performed in every patient with gastric symptoms in an effort to discover these precancerous states, and (b) all such patients are examined periodically by the x-ray and the gastroscope, despite the absence of symptoms referable to the stomach. Cases 3 and 4 demonstrate the value of periodic examinations in patients with extensive gastric atrophy in the early recognition of gastric cancer.

Case 3: An attorney aged 58 years had complained of indefinite gastrointestinal distress for twenty years. Several gastric analyses during the past ten years had revealed no free hydrochloric acid after stimulation with histamine. During the past five years, the patient had become weaker and more easily fatigued. During the eight months preceding examination he had experienced pain in the epigastrium and aversion to food; there had been a weight loss of several pounds. Numerous roentgen examinations of the stomach had been made over a period of ten years. A tentative diagnosis of gastric

ulcer had been made, although no definite lesion was found. During the last three years, a very gradual drawing in of the greater curvature opposite the angulus was observed, and was interpreted as spasm. Review of all the x-ray films at the time of the present examination indicated a filling defect on the greater curvature of the lower pole of the stomach, the first sign of which had appeared three years previously, and which had slowly increased.

Gastroscopy revealed a polypoid, nodular, nonulcerated, sharply defined tumor of the greater curvature of the antrum, extending toward the lower pole of the stomach. The nodes of its surface were variable in size. There was a complete atrophy of the gastric mucosa from the cardia to the pylorus (Fig. I). The gastroscopic diagnosis was that of a polypoid carcinoma (type I) of the greater curvature of the antrum, which had slowly developed on the soil of a severe atrophic gastritis. At operation, the tumor was found in the area described gastroscopically, and a resection was performed.

Microscopically, the tumor showed early malignant degeneration of a gastric polyp, and a severe atrophic gastritis involving the entire resected specimen.

Comment. There seems little doubt, upon review of the case history, that the development of a polypoid carcinomatous tumor was preceded by a chronic atrophic gastritis of at least ten years, and possibly twenty years, duration. It is questionable whether the very small filling defect present three years previously was evidence of a malignant tumor. It seems more logical to assume that at first a very small benign tumor developed in the presence of an atrophic gastritis, and that this benign lesion only recently degenerated into cancer.

Case 3. A man aged 59 years had suffered progressively increasing weakness with ascending numbness in the lower extremities for three years. At the onset of symptoms, a diagnosis had been made of pernicious anemia with combined cord degeneration. Liver extract had been prescribed, but was taken irregularly. Two months previously, he had been observed in another hospital and had been treated with liver extract and blood transfusions. No definite gastric symptoms were present but a roentgen examination of the stomach, made in the course of a routine study, was said to have demonstrated a filling defect in the prepyloric region (examination of the films later indicated that the apparent defect was produced by pressure of the spine). There had been a loss of 15 pounds in weight in the past two months. The patient's appetite remained good, however. Roentgen examination of the stomach was reported as normal, but gastroscopy was advised in view of the x-ray diagnosis of carcinoma, made elsewhere.

At gastroscopy, a normally functioning pylorus was seen. A gray atrophic patch was noted above the muscular sphincter antri. When the objective was turned toward the posterior wall of the mid-portion of the stomach a prominent tumor appeared in the visual field. It was limited by a wall, the edge of which appeared necrotic. There was no demarcation toward the posterior wall, and the tumor extended gradually into the neighboring darkened mucosa. A small polypoid tumor was seen toward the greater curvature separated from the tumor mass by a bridge of normal mucosa. Diagnoses were made of (1) type III carcinoma of the mid-portion of the posterior wall near the greater curvature, and (2) atrophic gastritis. A second roentgen examination was again negative. At operation, a small tumor was found in the mid-portion of the stomach on the posterior wall, close to the greater curvature. There was no evidence of metastases and a subtotal gastrectomy was performed. The microscopic diagnosis was adenocarcinoma of the stomach.

Comment. In this case, an early gastric cancer was diagnosed because a patient with pernicious anemia was examined gastroscopically in spite of the negative roentgenologic studies. There were no symptoms definitely referable to the stomach. However, the roentgenologist advised gastroscopy despite his normal findings, which demonstrates the importance of close cooperation between roentgenologist and

Figure II

Polypoid type I carcinoma in a patient with pernicious anemia.

gastroscopist. It is possible that a smaller lesion would have been detected had this patient been gastroscoped earlier. Figure II demonstrates a similar lesion occurring in another patient with pernicious anemia.

DIFFERENTIAL DIAGNOSIS OF BENIGN AND MALIGNANT GASTRIC ULCER

The differential diagnosis between benign and malignant gastric ulcer often is one of the most difficult problems which confronts the physician. Small ulcerating carcinomas not only may masquerade successfully as benign ulcers, but also may respond equally favorably to medical treatment. The prompt recognition of such lesions offers one of the most

favorable opportunities for the early diagnosis of gastric cancer. This can be achieved by repeated roentgenologic and gastroscopic examinations of all patients with gastric ulcer undergoing medical management.

Gastroscopy often permits the correct differential diagnosis by providing information regarding the color, conformation and extent of an ulcer, and by determining the presence or absence of infiltration of the surrounding mucosa. A benign gastric ulcer (Fig. III) appears gastroscopically as a bright white or yellow-white area in an orange-red field. The ulcer usually is round, though it may be elliptical. The edge is always sharp and punched out, even if its contour is irregular. It does not merge into the surrounding mucosa. The floor of the ulcer is always depressed, and may be flat or crater-like. It is covered with an adherent membrane, yellow-white or brilliant white in color. Fresh blood occasionally can be observed oozing from the base of the crater. Folds of mucous membrane often converge toward the edge of the ulcer. The adjacent mucosa may be normal, or inflamed and edematous.

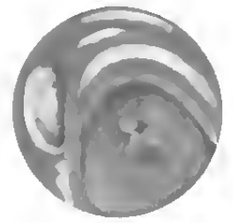
The malignant gastric ulcer usually presents a markedly different appearance. Its floor is irregular, and dirty-gray, brown, red, or violet in color. Its edge, or a portion of it, is ragged and irregular, and the transition between ulcerated and nonulcerated tissue is more gradual. The surrounding mucosa often is ridged, infiltrated and grayish-white, rather than the normal orange-red.

Cases 5 and 6 illustrate the importance of gastroscopy in the differentiation between benign and malignant gastric ulcer.

Case 5. A man aged 51 years had experienced gnawing epigastric distress, after meals, for three years, relieved by food and alkali. There had been no loss of weight. Free HCl was present in the gastric content after stimulation with histamine. The stools contained occult blood. Seven roentgen examinations of the stomach were performed during a period of five months, and demonstrated and followed the course of a large penetrating ulcer of the cardiac end of the lesser curvature. The third and fourth examinations showed a marked decrease in the size of the ulcer during antacid therapy. The first gastroscopic examination revealed a sharply defined ulcer on the lesser curvature, filled with coagulated blood. In this clotted blood, there was visible a grayish, ridge-like prominence. The gastroscopic diagnosis was that of ulcer-like carcinoma, since such a ridge-like prominence had not been seen in a benign ulcer. A second examination confirmed the original diagnosis especially since the ulcer was observed on an elevated area and one part of its edge was not sharply defined. Surgery was performed when the roentgen examination concurred in the diagnosis of carcinoma, and an ulcerating carcinoma of the lesser curvature was resected.

Case 6. A woman aged 51 years had experienced cramping epigastric distress for two years. During the last six months the pain had become sharp and gnawing; it occurred every two hours and was relieved by food and baking soda. There was no loss of weight. Four roentgen examinations followed the course of an ulceration on the lesser curvature in the region of the angulus. The ulcer crater decreased markedly in size during antacid therapy, but an area

Figure III



Typical benign ulcer on lesser curvature of the stomach just above the angulus.

of infiltration was observed involving the lesser curvature of the stomach and a definite roentgen diagnosis of ulcerating carcinoma was finally made. Three gastroscopies were performed during this period of observation. The initial examination revealed several moderately stiff folds converging toward a deep, round, grayish ulcer. Several stiffened nodes were present proximal to the ulcer, along the lesser curvature of the antrum. The appearance of the lesser curvature of the antrum and the angulus suggested an infiltrating lesion. The gastroscopic diagnosis was type III ulcerating carcinoma. A marked decrease in the size of the ulcer crater was noted at the second and third gastroscopic examinations, but, because of the persistent, irregular infiltration surrounding the ulcer, the original diagnosis of carcinoma was maintained. At operation, an ulcerating carcinoma was found on the lesser curvature of the stomach. A subtotal gastrectomy was performed.

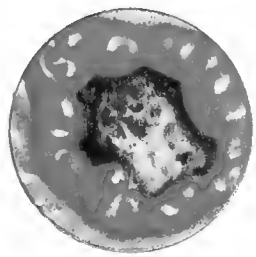
Comment. Both cases demonstrate the value of gastroscopy in establishing a positive diagnosis of malignancy at the initial examination, despite the fact that the lesions appeared benign clinically. The importance of repeated roentgenologic and gastroscopic examinations also is well illustrated.

DETERMINATION OF THE TYPE AND PROGNOSIS OF GASTRIC CARCINOMA

Four main types of gastric carcinoma are recognized gastroscopically. This classification, together with the location of the lesion, is of considerable practical importance in the determination of the opera-

bility and ultimate prognosis of gastric carcinoma. Type I is a sharply limited tumor supported on a broad base (Fig. I and II). Its surface contains numerous nodes and nodules of variable size. The color of the tumor normally is the same orange-red of the adjacent normal mucosa. Shallow ulcerations occasionally develop in the later stages. This type grows slowly and remains well demarcated. It occurs in 3% of the carcinomas observed gastroscopically. Its removal offers an excellent prognosis.

Figure IV



Type II carcinoma on lesser curvature of stomach.

The differentiation between polypoid carcinoma, benign tumor and giant hypertrophic gastritis at times may be difficult. The nodules of the surface of a benign tumor are regular and uniform in size, in contrast to the irregularity observed in a malignancy. Giant hypertrophic gastritis is characterized by a widespread and marked enlargement of the gastric folds. The very redundant mucosal layer, due to the active peristalsis of the tonically contracted underlying muscularis, may bulge into the lumen of the stomach, simulating a tumor. The softness of the gastric folds and their diffuse symmetrical enlargement are important distinguishing features.

Type II (Fig. IV) is a rather large ulcer surrounded by an elevated wall which is sharply demarcated from the surrounding mucosa. The color of the wall usually is dark red. The floor of the ulcer is irregular, covered with pieces of necrotic tissue, and may assume a dirty-gray, brown, red, or violet color. Type II is found in 18% of gastric carcinomas. Its removal offers a good prognosis.

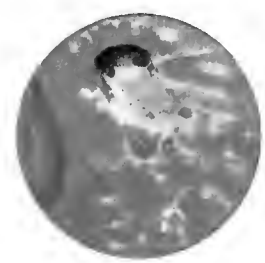
Type III consists of an ulcer which lies in the center of a prominent elevation. The floor usually is white in color. In the early stages, when the elevation is not yet marked, the lesion may be sharply circumscribed; the floor, however, is not as regular as in a benign ulcer. In later stages, the sharp limitation between ulcer and surrounding mucosa disappears either partially or completely (Fig. V). The ulcer wall may be so high that the ulcer itself is not visualized. This is particularly true in carcinomas of the lesser curvature. An ulcer in the pyloric region may be hidden by the infiltrated, prominent posterior wall; this rigid, often nodular, elevation is characteristic, however, and permits the diagnosis of carcinoma. Type III comprises 16% of gastric cancers. The prognosis remains doubtful even though the lesion appears operable.

Type IV comprises 63% of all gastric carcinomas. Two forms are distinguished: (1) the diffuse scirrhous infiltrations of the entire stomach, and (2) the partial infiltrations produced either by medullary or scirrhous carcinoma. The appearance is that of a stiff nodular, irregular surface. This type almost always offers a poor prognosis.

Even with the usual criteria of operability, gastroscopy is of value, as shown in the following case:

Case 7: A man aged 68 years complained of gnawing epigastric distress for eight months, and a loss of 21 pounds in weight in one year. Roentgen examination of the stomach revealed a constant irregularity along the greater curvature of the pars

Figure V



Type III carcinoma of the stomach. Note the indefinite transition of a portion of the ulcer into the surrounding infiltrated mucosa.

pylorica and pars media, which was apparently intrinsic and compatible with a diagnosis of carcinoma.

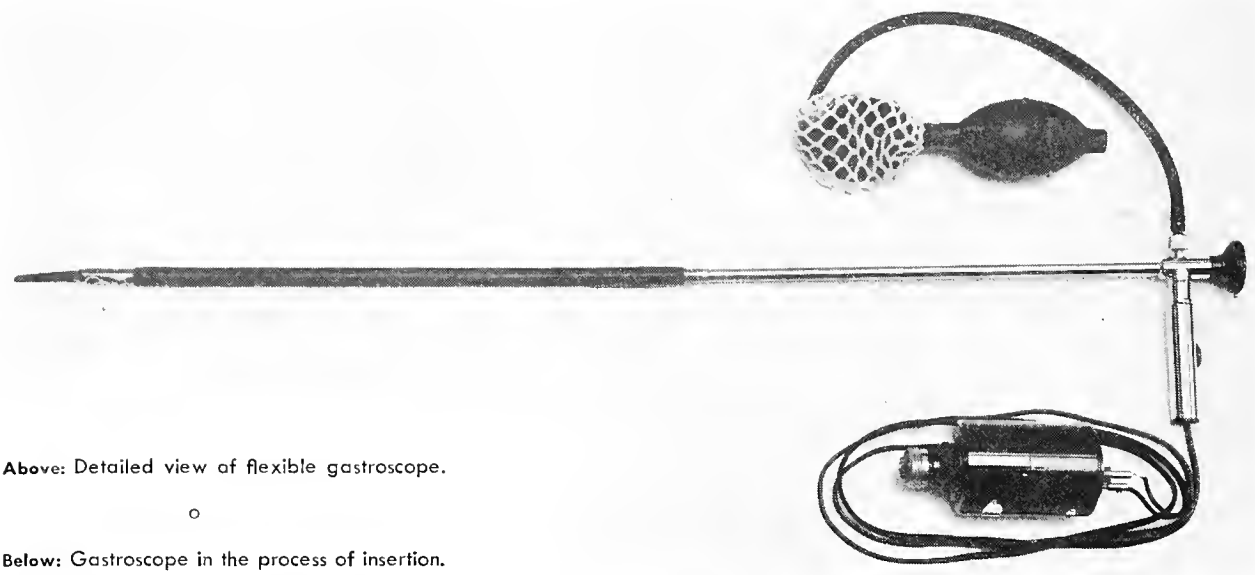
Gastroscopy disclosed a type II sharply demarcated carcinoma in the antrum, its upper margin lying at the level of the angulus. At operation, a large ulcerated lesion was found, with the infiltration apparently extending almost to the cardia. A very high subtotal gastrectomy was performed. The gross specimen showed what appeared to be almost complete carcinomatous involvement of the stomach. A firm mass was present in the region of the lesser curvature, near the pyloric end. The gastric wall appeared diffusely thickened, microscopic examination revealed a colloid carcinoma in the region of the pylorus and lesser curvature. No tumor cells were found in the thickened wall of the body of the stomach. The infiltration present there was inflammatory in character.

Comment: This case proved to be a type II carcinoma and confirmed the gastroscopic diagnosis as to site and operability. Roentgen examination indicated higher carcinomatous involvement and the gross examination seemed to confirm this. However, microscopic study showed that this apparent involvement was due to inflammation. This case, as

well as Case 2, emphasizes the fact that the gastroscopic appearance of a lesion occasionally may be more diagnostic than the surgical and gross examination.

CONCLUSIONS

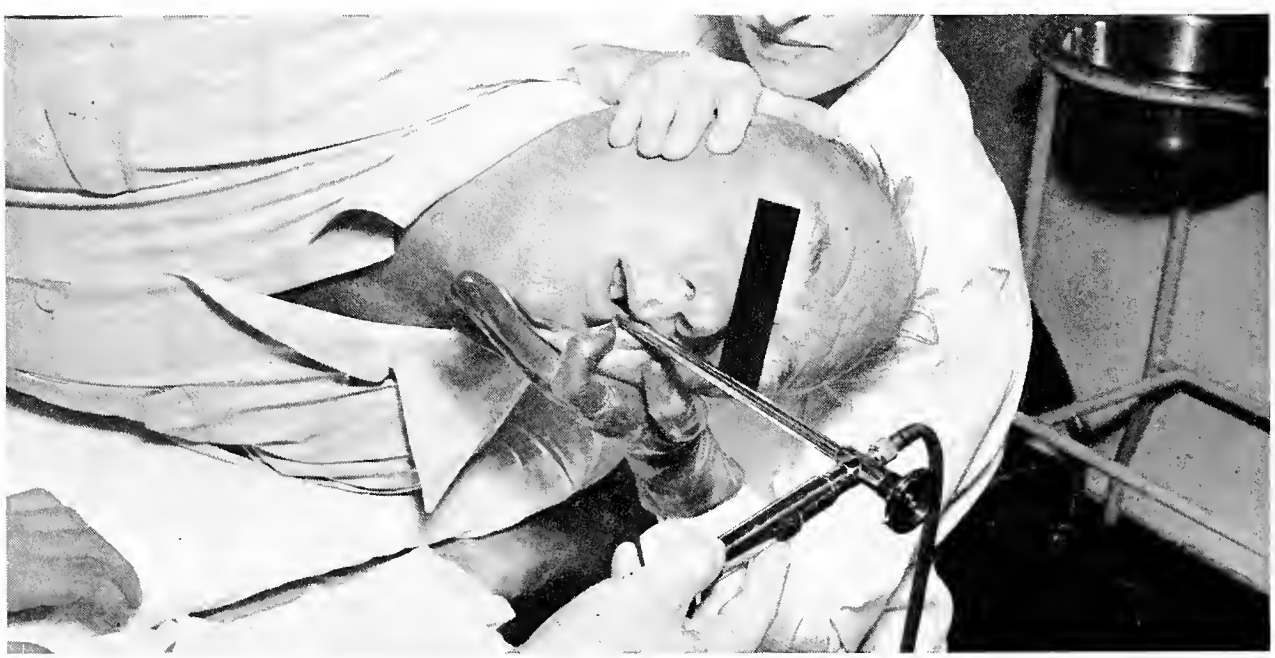
1. Gastroscopy is a valuable supplement to the roentgen examination of the stomach in the early diagnosis of cancer of the stomach.
2. It is indicated (a) in every patient with obscure abdominal complaints and unexplained loss of weight; (b) to clarify a doubtful roentgen diagnosis or confirm a positive diagnosis of carcinoma; (c) in every patient with gastric ulcer; and (d) to follow the course of chronic atrophic gastritis and gastric polyps.
3. Gastroscopy facilitates the differential diagnosis of benign and malignant gastric ulcer.
4. Gastroscopy provides important information regarding the type, location, operability, and prognosis of gastric carcinoma.



Above: Detailed view of flexible gastroscope.

o

Below: Gastroscope in the process of insertion.



Printed in U. S. A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. 1 NO. 12

EARLY DIAGNOSIS OF CARCINOMA IN THE GENITOURINARY TRACT

One reason for neglect in reporting signs and symptoms associated with lesions of the urinary tract is the patient's fear of a cystoscopic examination. In the past, this examination was performed without anesthesia and was a painful procedure, but with the advent of sodium pentothal, sacral block, and low spinal anesthesia, pain on examination need no longer be feared. Likewise, a false sense of modesty prevents many from reporting their symptoms early, but happily the younger generation has a more realistic attitude.

THE PENIS

Carcinoma of the penis occurs most commonly as a skin cancer, and differs little from the same lesion on other parts of the body. Pain is not an early symptom in most cases, and no characteristic symptoms are present. The outstanding feature of carcinoma of the penis is its chronicity.

The lesion usually presents an ulcer with a foul smelling discharge and occasional bleeding. A good rule to follow is this: Do a biopsy on any lesion of the penis which fails to show healing in three weeks, a test for syphilis having previously been taken and found negative. Regional adenitis is of little value in the diagnosis, because there may be infection which will also give rise to extensive adenitis.

An etiologic factor of great importance in carcinoma of the penis is a tight redundant foreskin which commonly predisposes to irritation and infection. Any patient past the age of 20 who has a nonretractable foreskin, or who complains of preputial irritation should be circumcised as a prophylactic measure. Statistical studies show that circumcision is of sound prophylactic value, even in elderly individuals.

Carcinoma arising from tissues other than the skin are rare in the penis. Occasionally a carcinoma in an old stricture is seen and differentiation from recurrent inflammation may be difficult.

THE TESTICLE

Enlargement of the testicle or a scrotal tumor is recognized early by the patient, because of a dragging sensation or a tightness noted in certain garments. Unfortunately, these patients frequently do not report this to their physician early because of the absence of pain. The vast majority of solid tumors of the testicle (97%) are cancerous. These solid tumors, restricted to the testicle in the early stage, usually present a smooth ovoid mass confined within the tunica albuginea. The benign tumors most commonly seen in the scrotum are cystic in type—hydrocele and spermatocele—and can easily be differentiated by palpation, transillumination, and aspiration.

The usual symptoms are swelling and pain; swelling is most frequent. After metastasis has occurred, loss of weight, nausea, and retroperitoneal masses may be noted.

Many of these tumors cause the excretion into the urine of an anterior pituitary-like hormone in sufficient quantities to be detected by the Friedman or Aschheim-Zondek test. A negative test does not preclude the possibility of cancer, however.

The diagnosis is made by palpation: The testicle is usually uniformly enlarged, hard, smooth, and heavy, but not particularly tender. Tuberculosis most commonly involves the epididymis. Long standing hydroceles or hematoceles, with thick walls, may be indistinguishable except by inspection or biopsy following surgical removal.

THE PROSTATE GLAND

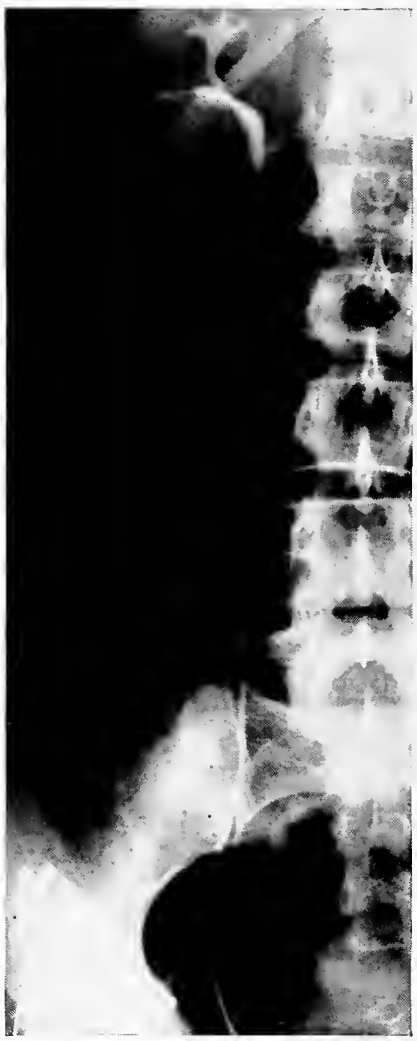
Carcinoma of the prostate gland occurs in 15 to 20% of all men past the age of 50. The incidence increases with age and may be as high as 30% in men past the age of 80. It is uncommon, although it may occur, in men under 50.

It can often be identified by rectal palpation, and is frequently associated with prostatic hypertrophy,

Figure I *(left)*. Tumor of testicle.

Figure II *(above)*. Early benign papilloma of the bladder.

Figure III *(right)*. Elongation of superior calix by outward growth of renal tumor.



although it also occurs in a normal sized gland.

Symptoms

In benign hypertrophy of the prostate gland, the patient has a gradual onset of symptoms, the average patient having had some dysuria for about seven years before consulting a physician. The symptoms of cancer of the prostate gland usually appear abruptly, and frequently the patient can recall the exact time of their initial appearance. The outstanding early symptoms are frequency and difficulty in urination (in benign hypertrophy the patient complains of slowness in starting and stopping of micturition, but has no discomfort).

Carcinoma of the prostate is likely to be irritative in character, whereas benign hypertrophy is usually obstructive. The passage of a catheter and the determination of residual urine will often reveal a small amount of residual urine, the symptoms being out of all proportion to the amount of urinary retention. Pain is uncommon in prostatic hypertrophy, but is a presenting symptom in about one third of the carcinoma cases.

Other symptoms of prostatic cancer arise from metastases which frequently occur before urinary obstruction takes place. Metastases involving the skeletal tissues produce severe pain in the lower back and along the sciatic nerve.

Diagnosis

Digital examination of the prostate gland per rectum is the most important factor in the diagnosis of this disease. Cancer of the prostate is characteristically of a stony hardness. Early, it may be present as a single nodule; late, the gland may be enlarged and fixed with its normal marking obliterated.

Roentgen examination of the sacral spine and the bony pelvis may reveal metastases. In the male, any condensing metastatic bone lesion arises either from a prostatic, thyroid, or kidney cancer, if Paget's disease can be ruled out.

Acid phosphatase has been demonstrated in the epithelial tissues of the adult prostate. In carcinoma of the prostate with metastasis, the phosphatase content of the blood frequently is markedly elevated.

Cystoscopic examination may be of some value in the diagnosis of cancer of the prostate. Marked distortion of the urethra is occasionally noted. Also, obstructive lesions may be differentiated, and biopsy be done for confirmatory study.

HEMATURIA

Blood in the urine may be gross or microscopic; it may be unassociated with other symptoms. Regardless of associated symptoms or findings, bleeding is a danger sign and should be given the same consideration as a red flag on an ammunition ship. All too frequently, we see patients who have had hematuria for months before consulting a urologist. Often the patient is to blame, because the bleeding was of short duration and he did not consider it important enough to report to his physician. Occasionally the physician gives the patient a urinary antiseptic, the bleeding stops, and he wrongly concludes that the bleeding was due to an acute infection. 70% of patients with hematuria suffer from serious disease, such as cancer, stone, nephritis, or infection. About 40% of patients with hematuria have a tumor somewhere in the urinary tract. It is noteworthy that a study of a large number of bladder tumors showed that the average patient did not consult a urologist until one and a half years after his first attack of bleeding.

THE BLADDER

Hematuria is the most prominent early symptom in most cases of bladder cancer. Later in the disease, obstructive symptoms may intervene, and still later, infection leads to a train of irritative symptoms, such as pain, urgency, tenesmus, and spasm. Not infrequently, prostatism may be coincidental with bladder cancer, but it is erroneous to assume that the bleeding is due to prostatic hypertrophy. Renal insufficiency may be present because the tumor has a tendency to locate on the trigone of the bladder and produce obstructive lesions at the ureteral orifice.

Every patient with hematuria should have a cystoscopic examination. This can be done painlessly with the newer anesthetics; biopsy can be done at the same time if deemed necessary. If the tumor is small, and suitable for transurethral fulguration, treatment can be carried out at this time.

It is advisable to do the cystoscopic examination while the patient is still bleeding, because the source of the bleeding is then more readily found. Many tumors of the bladder are thought to be benign in their beginning, but undergo malignant changes as they increase in size. There is no doubt that bladder tumors in their early phases are localized lesions which can often be eradicated by simple means.

THE KIDNEYS

Tumors of the renal parenchyma are almost always malignant and unilateral. Of the solid tumors of the kidney, 95% are cancerous. Most common is the adenocarcinoma, usually called hypernephroma.

It is noteworthy that renal tumors grow rapidly, invade the surrounding structures, and metastasize thru the blood stream. In about one third of these tumors the patient presents himself complaining of symptoms due to metastatic lesions. Frequently these symptoms are of nonurologic nature.

Symptoms

The first and most important symptom is painless hematuria, intermittent in character. The presence of a tumor in the renal area may be recognized. Pain of a colicky type, due to temporary ureteral obstruction by clots, is not infrequent. Dull aching pain may be due to tension on the renal capsule, or to nerve root involvement. Occasionally, low grade unexplained fever may be due to ischemic necrosis occurring in a fast growing mass. Wilms' tumors, occurring in children, seldom bleed, but swell to a great size; fullness in the renal area may be the first sign of the disease.

Flat x-ray films of the kidneys, ureters, and bladder may visualize the outline of the kidneys, psoas muscle, and the liver border. A lobulated or irregular outline of the kidney may indicate a tumor. Intravenous urography is a simple procedure and greatly facilitates the early diagnosis of many of the tumors. Not infrequently, it gives a differential test of kidney function, and outlines deformities of the calices and renal parenchyma and pelvis. However, absence of findings in the intravenous program does not preclude the possibility of a renal tumor.

Cystoscopy and retrograde pyelography should always be done, because it permits sharper contrast and makes fine details of deformity more manifest. These defects are of two types: (1) pressure or filling defects, with complete exclusion of one or more calices, and (2) elongation or stretching of calices, resulting in outward growth of the tumor. Occasionally, filling defects may be indefinite, resulting from blood clots or infection or nonopaque stone. When this occurs, repeated examination by retrograde pyelogram, after a few weeks, usually confirms or refutes a diagnosis of tumor.

APPLIED BIOPSY IN THE EARLY RECOGNITION OF CANCER

It was Virchow who demonstrated that a correlation exists, in most disease entities, between the clinical aspects of a condition and morphologic changes in the cells of the affected part. This finding gave rise to that special branch of pathology known as *cellular pathology*.

Microscopic examination of cellular structure was at first largely confined to parts removed at surgical operation or autopsy, but it soon became obvious that there was a broader field for such examinations in clinical practice. Small pieces of tissue could be removed from living patients and be subjected to pathologic examination for purposes of exact diagnosis and determination of definitive procedure in therapy. This operation became known as *biopsy* or *exploratory excision*. It is applicable, of course, only to tissues open to direct inspection, such as the skin, accessible mucous membranes, and parts exposed during surgical procedures.

HISTORICAL

The credit for introducing biopsy as a diagnostic method cannot be given to any one person. Biopsy methods were utilized by many practitioners, quite independent of each other, found good and promoted as valuable procedures. Eventually, more or less standardized technics were developed.

Although biopsy is today recognized as an indispensable diagnostic aid, it met with great opposition during its introductory period. This opposition came not only from the lesser lights in medicine but from those of high repute, as well.

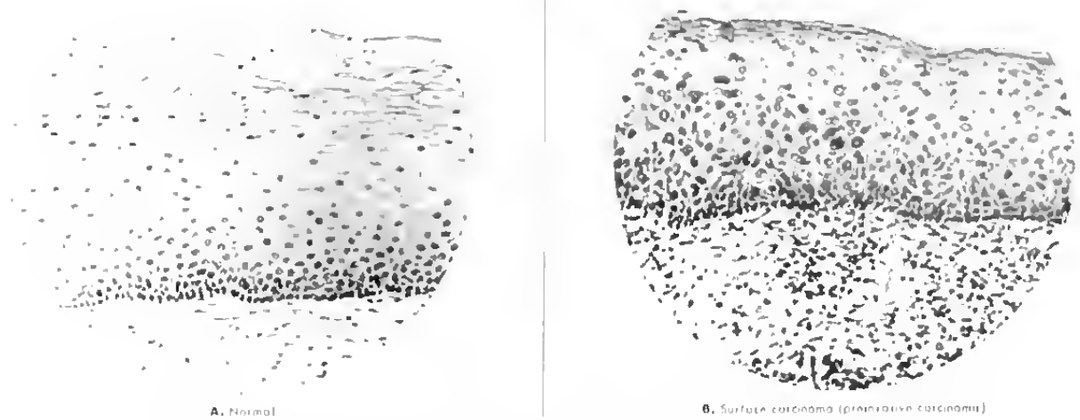
Olshausen, one of the most prominent gynecologists in the late 19th century, called the attempt to arrive at conclusions about an affected organ by microscopic examination of a small bit of tissue a shameful misconcept which conscientious surgeons never would be guilty of applying. Others warned that in the course of biopsy veins or lymph channels might be opened allowing germs or cancer cells to enter them, thus promoting general infection or metastatic cancer—a risk far surpassing the questionable diagnostic value of the method.

THE RISK INVOLVED

The value of biopsy is no longer questioned. However, even now occasional experiences seem to substantiate the claims of some of the early objectors. Cases are reported, by reliable observers, in which septicemia or metastases to remote organs developed soon after biopsy.

The connection between biopsy and septicemia or metastasis is suggested by the succession of events, but coincidence cannot be ruled out. The concept of cause and effect can be supported if bacteriologic cultures from the site of biopsy yield the same organisms as cultures from the blood stream, but even this does not positively rule out coincidence.

Stratified Epithelium From Two Surface Areas of the Same Cervical Polyp



A. Normal. B. Surface carcinoma (primitive carcinoma)

Note the irregularity of structure in B, the mixture of pale vesicular and dark hyperchromic nuclei, of small and large nuclei, and the presence of large nuclei on the superficial strata. Also note the absence of glycogen-storing surface stratum, and the inflammatory infiltration of the subepithelial stroma, which is always present beneath surface carcinoma.

Even less convincing is the assumption of cause and effect when metastasis is noted soon after biopsy on a cancerous tumor. Aside from the lack of direct proof, the incidence of this finding is so rare, in view of the enormous number of biopsies performed every day throughout the world, that it can claim little significance. Certainly it cannot be counted as a contraindication to the use of the method. When compared with the risk of other generally used procedures (general anesthesia, for instance) the risk is slight. If care is exercised to avoid squeezing or pressing the affected tissues, risk of metastasis is practically eliminated. Aseptic technic and local antiseptic application render the risk of septicemia almost negligible.

In order to reduce the risk to the absolute minimum, some surgeons perform biopsies only when the stage has been set for immediate complete extirpation of the affected part, in case the excised tissue proves to be cancerous. Making a quick frozen section of the tissue, followed by immediate microscopic examination by a pathologist makes it possible to provide the surgeon with a diagnosis in such a short time that he can hold up the operation and be guided by the new information in the completion of the surgical procedure. Frozen section diagnosis is commonly used in tumors of the breast.

Whether or not the removal of a cancer-infested organ immediately after biopsy will reduce the probability of septicemia or metastasis is debatable. There is one important advantage associated with the latter procedure, however: The patient is anesthetized but once, and undergoes only one operation, instead of two.

TECHNIC

There are four chief methods for doing a biopsy: (1) scalpel excision, (2) punch excision, (3) curettement (for the endometrium), and (4) sharp spoon scraping (for preinvasive surface carcinoma of the uterine cervix).

When the tumor presents a cauliflower, papillomatous, exophytic type of growth, a good specimen may be obtained by cutting a pedicle with scissors.

If a thermocautery is to be used, it should be used *after* the specimen has been obtained. The heat from the cautery may distort the histologic structure of the tissues for several millimeters from the area of application and thus interfere with obtaining a good specimen.

Scalpel Excision

Surgical excision of a piece of tissue with a scalpel is the method of choice, because it permits adaptation to particular conditions in any individual patient. The size of the piece to be removed and the location from which it is to be removed can be accurately controlled. This method provides the most information and best results.

Location.—In superficial lesions it is usually better to excise tissue from the peripheral portion rather than the central. The center represents the oldest part of the tumor and is frequently necrotic because of inadequate vascularization; the marginal portions are newer, more vascular, and give better information as to histologic structure.

Demarcation of the normal tissue from the pathologic presents entirely different pictures in various lesions and various organs, which are valuable clues for the pathologist. Hence, it is distinctly advantageous to include some contiguous normal tissue with the specimen of tumor or ulcer excised. This also holds true when lymph nodes are removed for diagnostic examination. In a group of affected lymph nodes it is not necessarily the largest which gives the best information. The centers of the larger nodes may have become necrotic and their peripheral subcapsular parts replaced by scar tissue. A small lymph node may provide a clearer and simpler microscopic picture, and the excision is often simpler than removal of a large one.

Size.—Do not be too chary about the size of the biopsy specimen excised. A few extra millimeters in diameter will mean nothing to the patient or the surgeon, but may be of great importance to the examining pathologist.

Punch Excision

When biopsy is accomplished with a punch instrument, the size and shape of the excised part cannot be regulated; it is determined by the instrument used. This drawback to the method is not serious in tumors of considerable mass, but in some lesions the restricted applicability of the instrument compels the surgeon to take a specimen from a part which is not the best for histologic examination.

Curettement

The usual curettement involves removal of the endometrium by scraping with a loop shaped instrument, one side of which is somewhat sharpened. This operation is admissible only on a tissue with strong regenerative powers, such as the endometrium. The cervical mucosa does not possess the regenerative powers of the endometrium: when curetted, voluntarily or involuntarily, infection may follow or ensuing scar formation may seriously interfere with cervical dilation at a later time.

Suction curettage.—Small pieces of endometrium may be removed by a suction apparatus—a simple and nondisabling maneuver. The advantage in this method is that it can be repeated at short intervals—daily, if necessary. It yields satisfactory information concerning the part of the endometrium from which the specimen was obtained, but does not rule out the possibility of important changes in other parts of the endometrium, perhaps only a few millimeters distant. Generally speaking, positive findings of cancerous tissue are convincing, but negative findings are meaningless. Hence, if carcinoma is suspected, suction curettage may be tried; if the findings are negative, complete curettage of the endometrium

should be done and the scrapings be carefully examined.

Scraping of the Cervix

When the Schiller test shows a suspicious white area on the cervix, a specimen may be obtained from the epithelial surface by scraping with a sharp spoon, similar in size and shape to the instrument used in operations on the mastoid. The spoon should have a razor-sharp edge, because a blunt instrument destroys the tissue structures.

In some instances, when the suspected area is not too small, it may be possible to peel off the epithelium with tissue forceps after having made an incision through the epithelium about the perimeter of the area. This maneuver affords a clue as to the nature of the lesion: The connection between carcinomatous surface epithelium and the stroma is much less firm than in like normal tissues. Peeling of the normal epithelium, in most cases, is difficult.

FIXATION OF THE SPECIMEN

Specimens removed at biopsy are small in volume with a relatively large surface area. Hence, they dry out quickly. Drying makes histologic examination difficult or even impossible. The excised tissue should, therefore, be placed in a fixation fluid immediately after removal.

It is not good practice to wrap the specimen in gauze. Gauze, like blotting paper, absorbs fluid. Very small specimens, thus wrapped, may become dry and shrunken within a few minutes.

A watery solution of formalin (8% to 10%) makes a satisfactory fixation fluid. Tissues may be left in such a solution for several days without danger of deterioration.

The addition of magnesium acetate, 2%, to an 8% solution of formalin provides a fixation fluid which prevents the swelling which pure formalin solution provokes in all tissues. This fluid also preserves the plasma cells, which are valuable indicators of inflammation, so that they will take special stains, such as methyl green pyronine by Unna-Pappenheim. Pure formalin destroys the acid proteins in plasma cells, rendering them unreceptive to special stains.

CLINICAL DATA

All the clinical data available should be submitted to the pathologist along with the biopsy specimen. The evaluation of some similar histologic changes may vary depending upon the organ in which found. Experience has shown that changes sufficient to justify a diagnosis of cancer, when found in one organ, may not justify a similar diagnosis when found in another. History may have a decisive bearing on the correct interpretation of findings in biopsy.

Biopsy is not done for the purpose of testing the pathologist; he should not be left to guess why and from what organ the material was obtained. Biopsy is done for the benefit of the patient and the information of the physician in charge. The pathologist is always anxious to do his best but frequently is not able to do so because of insufficient clinical data at hand.

BIOPSY IN VARIOUS ORGANS

The Skin.—In some organs the demarcation or line of cleavage between normal and carcinomatous cells is a sharp one. In most hornifying carcinomas of the skin, however, the transition is gradual. Hence evaluation of changes in the surface epithelium is made much easier if a piece of normal epithelium is included in the biopsy specimen when such a cancer is suspected. Basal cell cancer of the skin, on the other hand, usually shows a sharp line of cleavage, analogous to surface carcinoma of the uterine cervix.

The Larynx and Pharynx.—These organs afford good examples of a foregoing observation that similar changes must be evaluated differently in different organs. Certain epithelial changes, when found in the pharynx or larynx, have no significance so far as cancer is concerned, but similar changes in the stratified epithelium of the uterine cervix indicate a surface carcinoma.

The Rectum.—A high percentage of rectal cancers originate from polyps. A great many rectal polyps showing no gross evidence of cancer will, on microscopic examination, show evidence of early carcinomatous changes. For this reason, all rectal polyps should be removed and subjected to pathologic examination.

The Mammary Glands.—Nodes in the breast should be removed as soon as possible after discovery, and be microscopically checked, even though the history shows no progression in size over a period of time. Solitary nodes are more apt to be cancerous than multiple, isolated ones.

The Vulva.—Cancer of the vulva is a particularly insidious affair. The incidence of final, complete recovery is low compared with cancer in other organs which are open to direct inspection. The probable reason for this is that cancer of the vulva, in its earlier phase, may manifest itself in various forms. It may appear as an exophytic growth like a cauliflower wart, as a shallow ulcer, or as a thickening of the epithelium presenting the clinical picture of leukoplakia. When any such changes are observed they should be checked by biopsy. Unless this is done, much time may be lost in unsuccessful conservative treatment.

The Uterine Cervix.—Surface carcinomas of the uterine cervix may be discovered by Schiller's iodine test. After applying the iodine, the biopsy is done with a sharp spoon or by scalpel excision. The tissue removed should contain part of the white and part of the brown-stained epithelium. Areas around the external os with a dull, deep red surface are not to be examined by the iodine test because of the absence of stratified epithelium. Differential diagnosis between benign erosion and small ulcerative carcinoma can be determined only by the biopsy.

Printed in U.S.A.

The North Carolina Cancer Bulletin

Presented to the physicians of North Carolina by the Division of Cancer Control of the North Carolina State Board of Health, in cooperation with the Committee on Cancer Control of the North Carolina Medical Society and the North Carolina Division of the American Cancer Society. Originally published by the Committee on Cancer of the Illinois State Medical Society, with the financial aid of the Illinois Division of the American Cancer Society, in the interest of the earlier recognition of cancer.

NORTH CAROLINA STATE BOARD OF HEALTH
Division of Cancer Control
Raleigh, North Carolina

EARLY CANCER IS CURABLE

VOL. 1 SUPPLEMENT

HEREDITY AND CANCER

A Résumé of Experimental and Clinical Studies

(Editor's Note: For the sake of completeness, and for the information of those who may have a special interest in the question, the following article is submitted to inquiring readers of The Cancer Bulletin. *It is based on material supplied by the director of cancer research at a large hospital, and represents a summation of present knowledge on a still controversial subject. The hereditary aspect of cancer in mice has been rather definitely worked out; in man, it is still in the hypothetic and conjectural stage.)*

THE PROBLEM

A patient comes to you and says, "My father and a grandmother died of cancer," then asks, "Will I develop cancer?" A young woman wants to know, "My mother and sister had cancer of the breast; is it safe for me to marry and have children?" A man inquires, "My brother, an identical twin, has cancer of the stomach. Should I be examined for cancer?"

What are you going to tell these people? Is the information available on which to formulate intelligent answers to their questions?

In an attempt to supply such information, scientists have studied and are studying intensively the influence of heredity on cancer. In man, the problem of heredity may be stated thus: What is the chance of a particular person developing cancer in his lifetime? But first let us review what has been learned about heredity of cancer in mice.

HEREDITY OF CANCER IN MICE

The study of cancer heredity in the mouse also begins with the question: What is the probability of a given mouse developing cancer? To answer this question, the first thing that must be known is the family history of the particular mouse.

Scientists have inbred mice to obtain pure strains. These mice have been assigned code names such as C3H, C57 black, and A. Mice of different strains vary in their chances of developing tumors. Mouse Alberta has a mother and father belonging to the C3H strain. Her chance of developing cancer of the breast in a normal lifetime is very high, 92% or 92 out of 100. Her brother Albert has less than 1% likelihood of dying from breast cancer.

Mouse Barbara and brother Baldwin of strain A have a high probability of getting a tumor of the lung (90%) but only a slight chance of breast cancer (5% or less). (Mouse Barbara's slight chance of having cancer of the breast depends, of course, upon her remaining a virgin. If she is bred, her chance of having breast cancer rises to 84%, and she is more apt to succumb to cancer of the breast than of the lung.) Caroline of strain 1 will surely develop tumors of the stomach (100%). Dinah of strain C58 will probably die of leukemia (90%). Frederick and Frederica are particularly fortunate: Their parents were C57 leaden, and their chance of developing cancer of any kind is less than 1%.

In these experiments on mice, under controlled conditions, the type of tumor and the chances of developing cancer depended upon the family history. The mice did not, apparently, have a susceptibility to cancer in general but only a tendency to develop certain specific types of cancer. The resistance of an animal to breast cancer does not mean that the animal is more or less susceptible to sarcoma or leukemia.

Cancer of the Lung in Mice

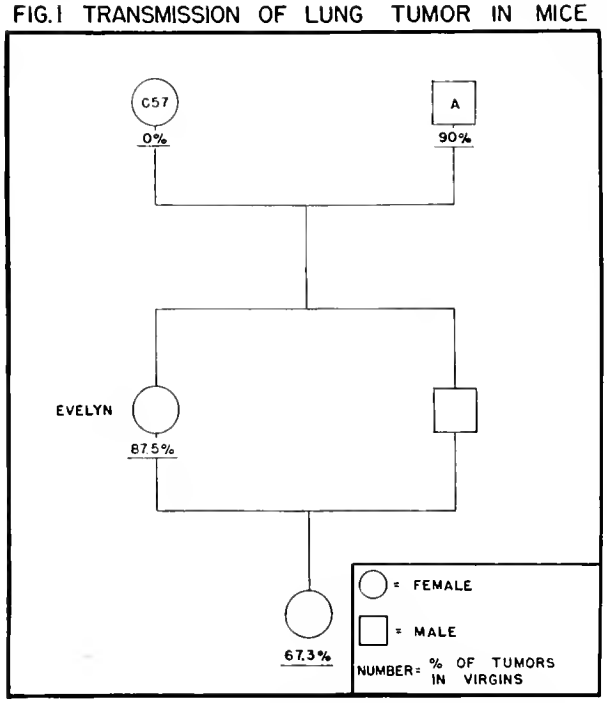
So far the problem in mice has been simple. Both parents belonged to the same strain. A mouse tended to develop the same type of tumor as its ancestors. How does the mouse acquire its susceptibility to

cancer from its parents? To study this problem, the mother and father mouse should belong to different strains.

Mouse Evelyn had a mother of strain A and a father of strain C57 (see Figure 1). The chance of developing cancer of the lung is high in strain A and low for C57. Mouse Evelyn has an 87.5% chance of getting cancer of the lung. The children of Evelyn mated to her brother have a 67.3% chance of dying as a result of this tumor.

For comparison, let us mate a white female mouse and a black male. The children are black, in 100% of the cases. If the children (all black) are mated, the grandchildren are colored in 75% of the cases. This experiment is similar to the classical work of Mendel on the inheritance of color in peas. From

FIG. 1 TRANSMISSION OF LUNG TUMOR IN MICE



such experiments, scientists learn that the black color of the skin in the mouse is dependent on a gene acquired from the mother or father. Furthermore, the gene for the black color is said to be dominant over the gene for the white color.

The development of lung cancer in mouse Evelyn also seems to be largely dependent on a gene. Furthermore, the tendency to develop cancer of the lung in strain A and its hybrids seems to be a dominant characteristic. In this experiment, the susceptibility to cancer of the lung could be inherited either from the mother or the father. The mother did not have any greater tendency to transmit the susceptibility to cancer than the father.

In man, a few types of tumor seem to be transmitted by one or more genes. Intestinal polyposis is an example of such a tumor. The transmission of this disease from one generation to another is shown in the family tree of Figure 2. This tumor is, ordinarily, rare and it is no coincidence that such a large number of cases occurred in one family. Other types of tumor that are apparently inherited will be presented later.

Genes, however, are not the whole story in the transmission of cancer from parent to offspring. In certain tumors of the mouse, genes apparently play only a minor role. For this story, we have to consider cancer of the breast in mice.

Cancer of the Breast in Mice

Figure 3 shows a mother mouse of strain A with an 84% chance of developing cancer of the breast. The black father mouse belongs to strain C57 which develops few tumors. The daughter mouse, Harriet, like the mother, has a high chance of getting breast cancer.

Suppose the strains of the mother and father are reversed. This time the mother belongs to the strain C57 with a low percentage of cancer. The father is strain A with a high percentage. The daughter mouse, Irene, has the same genes as Harriet. But Irene, like her mother, has a relatively low chance of developing cancer (2%). Harriet, in contrast, has a high probability (95%).

The susceptibility to cancer of the breast in these mice does not depend on the genes alone but on the mother, also. It seems as if the mother is more important than the father in determining the chances of a daughter mouse developing cancer of the breast. But is the mother really important?

Milk Factor. Other experiments show that the susceptibility to cancer of the breast in a mouse does not necessarily depend on the mother.

Mouse Helen, a sister of Harriet, was removed from her high tumor strain mother at birth and was nursed by a foster mother of the low cancer strain C57 (see Figure 3). The chances of developing cancer of the breast were 0% in Helen but 95% in sister Harriet.

Irene has a sister Ida. Irene nursed by her own mother C57 has only a 2% chance of dying of cancer. Ida nursed by a mouse of the high tumor strain A has a 93% probability of cancer.

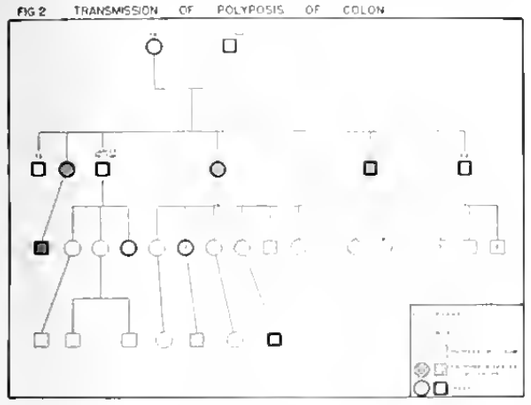
In these two experiments, the chance of developing breast cancer did not depend entirely on the mother or the father. Breast cancer in these mice depended primarily on the foster mother.

How does the foster mother influence the production of cancer in the children? It has been shown that the milk of the foster mother contains something (a virus?) which is transmitted to the infant mouse. This milk factor, ingested by the infant mouse, produces breast cancer one or two years

later in mice which have the genetic susceptibility. The factor is being intensively studied in many laboratories.

One can only speculate whether there is a milk factor in women. No such factor has been proved, either by experiment or by statistics. In spite of the

FIG 2 TRANSMISSION OF POLYPOSIS OF COLON



lack of proof, it might seem reasonable to advise women who have a family history of breast cancer not to nurse their infant daughters.

Environmental Factors

The type of tumor and the probability of developing tumor in mice depend, it has been seen, on the parents and on the foster mother. But that is not the whole story. Its chance of developing cancer increases or diminishes according to what happens to the mouse during its lifetime. The development of tumor depends not only on the family history but on the life history of the mouse, as well.

Pregnancy. Mary had a parentage of strain A, was nursed by her mother, and had a number of litters. Her chance of developing breast cancer was 84%. Her sister Mathilda remained a virgin through choice—the experimenter's choice. Mathilda's probability of breast cancer was only 5%. It was not virginity in itself, but lack of pregnancy and children, which paid dividends in a smaller chance of breast cancer.

In mice of strain A, the virgin females had much less breast cancer than the breeders (3%, as compared to 84%). In the C3H strain, there is no difference in breast cancer of virgins and breeders. Virginity or lack of pregnancy protects the A mice but not the C3H mice against breast cancer.

What about human breast cancer? According to some statistics, single women have a slightly higher incidence of breast cancer than married women. This finding does not seem to be in accord with the experiments on mice. There is a need for additional statistics on breast cancer in single and married women.

Female sex hormone. Sister Margaret also remained a virgin but she was treated with estrogen, the female sex hormone. Her chance of breast cancer was 91%, as compared to 3% for Mathilda. Breast cancer is rare in male mice (less than 1%). Martin, however, was injected with estrogen and he had a 33% chance of getting this tumor.

Estrogen increased the probability of breast cancer in Margaret and Martin. Injection of estrogen into mice of the tumor-resistant strain C57 does not, however, increase the incidence of breast cancer. Estrogen is dangerous only to those mice with a "bad" family history.

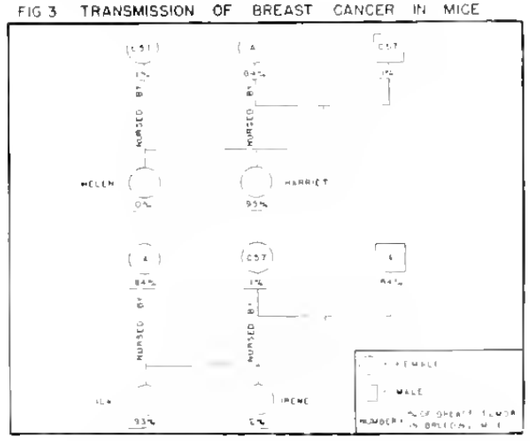
A few doctors have reported that breast cancers developed in men and women after heavy estrogen treatment. It may be worth while to avoid excessive treatment with female sex hormones in persons with a family history of breast cancer.

Diet. An important factor is diet. Rose, who was fed as much as she wanted, had a 90% chance of developing cancer of the breast. Her sister Ruth was fed a restricted diet. She had enough food to remain in good health but she did not become as heavy as her sister. Ruth's reward for dieting was a decreased probability of cancer of the breast, only 9% instead of 90%. Evidently dieting was worth while.

Breast cancer is not the only tumor that is prevented by diet. Restricted feeding decreased the incidence of lung tumor. Even tumors produced by chemicals are inhibited by diets. Investigators are studying whether restriction of any particular food will prevent cancer.

Do these results apply to human tumors? Statistics

FIG 3 TRANSMISSION OF BREAST CANCER IN MICE



collected from the records of insurance companies suggest that cancer occurs less frequently in slender people than in those who are overweight. But much more research has to be done before one can recommend diet as a means of cancer control.

HEREDITY AND CANCER IN MAN

An impressive amount of data has been accumulated on the relationship of heredity and environmental factors in the production of tumors in mice. The information on heredity in man is only fragmentary. Most of the information has been obtained by studying the families of patients with cancer.

Here is the problem we have to solve: If a person has cancer in his family history, does he have a greater chance of developing cancer than the average individual?

Patient M. S. gives a family history shown in the diagram. Of 13 deaths in individuals 30 years or older, 5 died of cancer. Does patient M. S. have a greater chance of developing cancer than the average individual?

This question poses a fundamental problem. Unfortunately, we cannot, at the present time, give a categorical answer. Our knowledge of the significance of cancer in the family history is slight. We are only beginning to learn how to analyze family histories.

Type of Cancer

What should we consider in the family history? First we must know the type of tumor. The knowledge that a relative died of cancer does not mean anything. We have to know where the cancer was and, if possible, the pathologic diagnosis of the tumor.

Some types of tumors are frequently inherited. Here is a list of some of the tumors that are frequently inherited:

Multiple polyposis of colon
Neurofibromatosis
Multiple chondroma
Retinoblastoma of the eye

These tumors are usually characterized by (1) occurring early in life and (2) being bilateral or multiple. Any of these tumors in the family history is a definite danger sign. The patient has a fairly high chance of developing the same type of tumor. Fortunately, all of these tumors are rare. Some of them are benign, but they may become malignant. If any of these tumors are found in a patient, relatives of the patient should be examined. Should members of such a family have children? Probably not, in most cases.

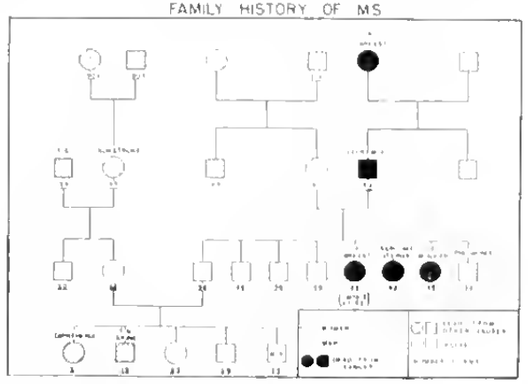
Some types of tumors may be inherited. This group includes cancer of the breast and internal organs—the uterus, stomach, large intestine, prostate, brain. It is possible that cancer of the rectum, bladder and esophagus should also be included. Cancer of the breast in a family history, for example, is supposed to increase slightly the chances of the individual to develop not only breast cancer but also other types of tumors. A family history with cancer of the internal organs is not, however, as dangerous or as significant as one with the hereditary tumors described above.

A family history of cancer of the internal organs should not cause undue alarm or worry. In fact, insurance companies do not pay any attention to a family history of cancer even when both parents died of cancer.

Some tumors are usually not inherited. This group includes cancer of the accessible organs—the skin, lip, mouth, larynx, penis, and cervix. These tumors are usually due to known and unknown environmental factors; heredity does not seem to be important. A family history of cancer of the accessible organs probably does not increase the susceptibility of a person to cancer.

Let us now consider patient M. S. His family history included individuals with leukemia, sarcoma of the uterus, cancer of the bladder, and breast cancer (2 cases). There were four different types of tumor—all belonging to the second group of cancer. These tumors may increase slightly the susceptibility of the patient to cancer. If all the five individuals had had the same type of cancer, it would be definite that the patient M. S. has an increased susceptibility to that tumor. The history of two women with cancer of the breast might, at first, appear significant, but both cases of breast cancer were on the father's side. Probably, neither M. S. nor his sister have acquired a "milk factor" (if such a factor exists in humans) for breast cancer.

FAMILY HISTORY OF MS



Number of cancers in family. But M. S. had 5 relatives with cancer. Is the large number of cases a proof that cancer is inherited in his family, or is it just a coincidence that there is such a large number of deaths due to cancer? According to cancer statistics, approximately one death out of ten after the age of 30 is due to cancer. The family of M. S. had 5 cancers in 13 deaths. The chance that these 5 cancers were due to coincidence is less than 1 in

100. Therefore, in the family of M. S., there is probably some factor (heredity?) which caused an unusually large number of cancer deaths.

Further examination of the family tree shows that all the cancer deaths were on the father's side, and none on the mother's. In the father's relatives, there were 11 deaths after age 40. Nearly half of them died of cancer. Clearly this high percentage of cancer deaths is not a coincidence.

The attached table may aid in the evaluation of a family history. It shows the number of cancer deaths required before one can consider that cancer is a significant factor in the family. For example, in a family with 14 deaths, 4 cancer deaths are suggestive and 5 cancer deaths are fairly definite evidence of some hereditary or other cancer factor in the family.

Number of Cancer Deaths That Would Be:		*Total*
Probably Significant	*Possibly Significant*	*Number of Deaths Past 40*
4	3	6 to 9
5	4	10 to 15
6	5	16 to 21

Let us now review the family history of M.S. Cancer seems to be a prominent disease in this family for the following reasons:

1. The types of cancer in the family history may be inheritable.
2. Two of the cancers affect the same organ.
3. All the cancers are present on the father's side.
4. The number of tumors are more than could be ascribed to coincidence.

Twins. The question of heredity of cancer is of particular importance when twins are considered. First it is necessary to know whether the twins are identical or not.

Non-identical twins develop from separate ova and sperms. They may be of the same sex or of different sexes. They do not have any closer relationship than brothers and sisters of any family. If a non-identical twin has cancer, the chance of the other getting cancer is the same as for another brother or sister.

Identical twins, however, develop from the same sperm and egg. They have then the same genes and the same inheritance. They are always of the same sex and resemble each other closely. Not only do the identical twins have the same heredity but usually they have the same environment. The occurrence of cancer in one twin indicates, it is believed, that the other has an increased chance of developing the same type of tumor in the same organ. Sometimes the same cancer attacks the identical twins at the same age. Therefore, the finding of cancer in one twin calls for an examination and continued observation of the other.

Individual history. Suppose the patient's family history is bad for cancer; what then? For example, let us say that the mother, an aunt, and a great-aunt died of cancer of the breast at 25, 30, and 50 years of age respectively. The patient has, in all probability, a somewhat greater chance of developing cancer of the breast than the average individual. But the patient's own history will determine to a large extent whether he or she will develop cancer.

What factors in the person's history will increase or decrease the chance of developing breast cancer? If we assume that the findings in mice on breast cancer are applicable to humans—a big assumption —we can give a partial answer to the question.

In the first place, if the patient is a man with a family history of breast cancer he has but little chance of developing this tumor. Suppose the patient is a woman with the same family history and suppose she had not been nursed by her mother, her chance of developing cancer of the breast is not much greater than those of the average woman. It probably would be inadvisable to administer excessive amounts of female sex hormones to such a patient. If she gave birth to girls, it might be worth while to advise her not to nurse them. Lack of nursing may increase slightly her own chance of developing cancer of the breast, but it will prevent the transfer to her daughters of any "milk factor" which may be present in human milk.

The most important thing the woman can do is to have periodic examinations. Then any precancerous condition that may develop can be eliminated. And if cancer does develop, it can be diagnosed early and treated early.

The person with cancer in the family history may or may not have a greater chance of developing cancer. If he is wise, he will become cancer-conscious but not cancer-phobic. By periodic examinations and proper hygiene, he will materially decrease his chances of succumbing to cancer. He may decrease his chances to such an extent that he may be better off than the average person.

Cancer in the family history is not a cause for alarm but an indication for caution.

ACKNOWLEDGMENTS

An undertaking such as the publication of THE ILLINOIS CANCER BULLETIN (the BULLETINS were originated and first published by the Committee on Cancer of the Illinois State Medical Society) could hardly be successfully executed without the generous co-operation of many experienced and interested persons. It is therefore a duty and a pleasure for the Editor to thank and give due credit to those who have given of their time and knowledge to the cause of the BULLETIN.

Authors: The general articles in the BULLETINS I to VIII were prepared by Erich Sachs, M.D., and Reuben L. Larsen, M.D., who also acted as co-authors in other instances.

Contributors: The special articles pertaining to the early diagnosis of cancer in individual fields of medicine were contributed by:

James T. Case, M.D., Passavant Memorial Hospital, Chicago, *Roentgenology*

James I. Farrell, M.D., Evanston Hospital, Evanston, Illinois, *Urology*

Paul H. Holinger, M.D., Research and Educational Hospitals, University of Illinois, and St. Luke's Hospital, Chicago, *Respiratory Tract and Esophageal Endoscopy*

Joseph B. Kirsner, M.D., Albert Merritt Billings Hospital, Chicago, *Gastroscopy*

J. Peerman Nesselrod, M.D., Evanston Hospital, Evanston, Illinois, *Proctoscopy*

Walter Schiller, M.D., Women and Children's Hospital, Chicago, *Biopsy*

Robert Schrek, M.D., Edward Hines, Jr., Memorial Hospital, Hines, Illinois, *Heredity*

Artist: Miss Lucille Cassell, Artist at Northwestern University Medical School, graciously contributed her time and talents.

Contributors of Illustrations: The number of excellent illustrations of early cancer that we have been able to secure and publish has been a special feature of the BULLETIN. Illustrations of late cancers are numerous and easy to obtain, but of little teaching value.

The authors of the special articles, indicated above, supplied illustrations. In addition, illustrations have been supplied by:

Earl E. Barth, M.D., Wesley Memorial Hospital, Chicago

Charles E. Galloway, M.D., Evanston Hospital, Evanston, Illinois

Paul H. Holinger, M.D., and W. VanHazel, M.D., St. Luke's Hospital, Chicago

Frank L. Hussey, M.D., Wesley Memorial Hospital, Chicago

Rudolf Schindler, M.D., Los Angeles County General Hospital, Los Angeles

Howard C. Taylor, Jr., M.D., and Robert Millen, M.D., Roosevelt Hospital, New York City

Erich M. Uhlmann, M.D., Michael Reese Hospital, Chicago

John Wolfer, M.D., Passavant Memorial Hospital, Chicago

The Editor is grateful to "What's New" for rendering it possible for the BULLETIN to exhibit illustrations in color. "What's New" made color plates of photographs secured by the Editor and gave the color plates to the Editor for use in the BULLETIN. The funds available to the Editor of the BULLETIN were too limited otherwise to allow for production and use of color plates.

Constructive Criticism: Doctors Ludvig Hektoen, J. P. Simonds, Bowman C. Crowell, and J. J. Moore have read the subject matter of each issue prior to publication. We thank these experts in pathology for their generous help.

Publisher: Finally, the Editor and the Committee on Cancer of the Illinois State Medical Society could not have produced the BULLETIN except for the various services which Dr. L. G. Maison of L. G. Maison and Company (of which Doctors Sachs and Larsen are part) placed at our command without cost.

PROSPECTUS FOR VOLUME II

The first volume of THE CANCER BULLETINS comes to a conclusion with this number. Volume I has been concerned chiefly with early recognition of cancer, emphasizing alertness and a suspicious attitude toward patients in the cancer age, because early cancer is usually curable.

Pursuing the same theme—the importance of early recognition of cancer—Volume II will continue, in an abbreviated form, to emphasize diagnosis. Concise, pithy articles by specialists in various branches of medicine will consider the pitfalls—the errors and oversights—which lead to wrong or missed diagnoses. Differential diagnosis will be the principal consideration.

Printed in U.S.A.